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NIH GUIDE for GRANTS and CONTRACTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Vol. 11, No. 1, January 1, 1982

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The GUIDE is published at irregular intervals to announce scientific initiatives and to provide policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in grants and contracts activities administered by the National Institutes of Health.

Two types of supplements are published by the respective awarding units. Those printed on yellow paper concern contracts: solicitations of sources and announcement of availability of requests for proposals. Those printed on blue paper concern invitations for grant applications in well-defined scientific areas to accomplish specific program purposes.

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ANNOUNCEMENT

ORGANIZATION AND FUNCTION OF THE NIEHS

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

The National Institute of Environmental Health Sciences (NIEHS) is the principal Federal agency for biomedical research on the effects of chemical and physical environmental agents on man's health and well-being.

The NIEHS is one of the Institutes of the National Institutes of Health (NIH). The only one located outside the Washington, D.C. area, it is situated in the Research Triangle Park, North Carolina. All operations and activities of the NIEHS are conducted within the framework of the NIH, and the Extramural Program functions within the purview of the Office of Extramural Research and Training, NIH. The Institute utilizes the Division of Resarch Grants (DRG) and national advisory groups for review of grant applications. Application forms, receipt dates, publication of announcements, notices and requests for applications (RFA) follow the standard NIH format and procedures.

Following assignment of applications to the NIEHS Referral Office, Division of Research Grants, an appropriate Initial Review Group (Study Section) selected by the DRG, reviews the Regular Research Grant, Program Project Grant, and Research Career Development Grant applications.

An alternative review procedure is used for Environmental Health Sciences Center, Marine and Freshwater Biomedical Center, Institutional Training, and Mid-Career Developmental grant applications which undergo initial review by an advisory group established by the NIEHS. Secondary review of all grant applications is carried out by the National Advisory Environmental Health Sciences Council (NAEHSC). The assignment of all grant proposals to the NIEHS, regardless of type, is through the Division of Research Grants, NIH.

Additional information concerning the mission and interests of the program of the NIEHS may be obtained by contacting the Office of the Director, Extramural Programs, NIEHS, P.O. Box 12233, Research Triangle Park, North Carolina 27709, Telephone (919) 541-7723, or Program Directors for specific programs as listed below:

Dr. Robert G. Owens Telephone (919) 541-7825	- Special Programs
Dr. Edward Gardner, Jr. Telephone (919) 541-7724	- Regular Research Grants
Dr. Christopher Schonwalder Telephone (919) 541-7634	- Research Manpower Development

ANNOUNCEMENT

AVAILABILITY OF SENIOR INTERNATIONAL FELLOWSHIPS FOR 1983-84

FOGARTY INTERNATIONAL CENTER.

The John E. Fogarty International Center for Advanced Study in the Health Sciences (FIC) announces the availability of senior postdoctoral research fellowships to U.S. health scientists who wish to study abroad. The purpose of these fellowships is to enhance the exchange of ideas and information in the various biomedical and behavioral disciplines. The types of activity that are supported by this program include collaboration in basic or clinical research, and the familiarization with or utilization of special techniques and equipment not otherwise available to the applicant. These programs do not provide support for brief observational visits, attendance at scientific meetings, attendance in formal training courses, or independent research projects within the host institution.

ELIGIBILITY REQUIREMENTS

Applicants must meet the following requirements:

- U.S. citizen or permanent U.S. resident;
- Doctoral degree in a clinical, biomedical or behavioral science;
- Five years or more of postdoctoral experience;
- Professional experience in the health or biomedical sciences for at least two of the last four years;
- Affiliation with a non-Federal U.S. public or private nonprofit research, clinical or educational institution.

APPLICATION AND SELECTION

Fellowship applications are reviewed once annually. The receipt date for applications to the Senior International Fellowship Program is June 1, 1982. All applications are reviewed for scientific merit by the National Institutes of Health. Fellowship awards are made for periods of three to twelve months. A fellowship can be activated within one year after receiving the Notice of Award and the starting date of the fellowship is set by mutual agreement between the applicant and the host institution.

Prospective applicants for the Senior International Fellowship Program may obtain information brochures from FIC. Only the dean or equivalent institutional official may request fellowship applications which will be available from Januuary 15 to May 15, 1982. Information and fellowship applications are available from:

International Research and Awards Branch
Fogarty International Center
National Institutes of Health
Bethesda, Maryland 20205

For an expedient reply, please send a self-addressed label to the above address.

ANNOUNCEMENT

THE GENETIC BASIS OF AGING

NATIONAL INSTITUTE ON AGING

INTRODUCTION

This announcement supersedes three preceding announcements by the National Institute on Aging: 1) The Genetic Basis of Aging: Drosophila as a Model System, NIH Guide for Grants and Contracts Vol. 7, No. 19, December 15, 1978, pp 23-25; 2) The Genetic Basis of Aging: Protozoa as Models, NIH Guide for Grants and Contracts Vol. 8, No. 8, June 5, 1978, pp 7-9; and 3) The Genetic Basis of Aging: C. Elegans as a Model System, NIH Guide for Grants and Contracts Vol. 9, No. 2, January 25, 1980, pp 51-54.

BACKGROUND INFORMATION

The National Institute on Aging (NIA) conducts and supports biomedical, behavioral, social, and clinical research, and research training related to the processes of aging and to the diseases and other special problems and needs of the aged. Genetic analysis is a powerful tool that can be applied to research on aging and longevity.

Research on human populations and human cells are encouraged where they are appropriate. In addition, many types of studies on the genetic basis of aging and longevity require experimental animals that can be maintained under controlled conditions and manipulated according to experimental protocols. Research on the genetics of aging and longevity using mammalian models is particularly encouraged by the NIA. However, research using lower organisms is also of interest to the NIA where understanding aging is the major focus of the project, where questions will be asked that cannot be examined readily in mammals and where there is evidence for physiological processes that parallel those seen in human aging.

GOALS AND SCOPE

The purpose of this announcement is to withdraw the three previous announcements described in the Introduction. Hence, this is not an announcement of a new program. A new program announcement concerning mammalian models for genetic research on aging will be made in the future.

This program is described in the Catalog of Federal Domestic Assistance Number 13.866, Aging Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered uner PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

INQUIRIES AND CORRESPONDENCE

Inquiries and correspondence should be directed to:

Dr. Richard L. Sprott
Chief
Molecular and Cellular Biology Branch
Biomedical Research and Clinical Medicine Program
National Institute on Aging
Building 31, Room 5C15
Bethesda, Maryland 20205

Telephone: 301 - 496-6402

ANNOUNCEMENT

RESEARCH GRANTS ON BRAIN DYSFUNCTION IN DISORDERS OF LEARNING

NATIONAL INSTITUTE OF NEUROLOGICAL AND COMMUNICATIVE DISORDERS AND STROKE
NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

The Developmental Neurology Branch, Neurological Disorders Program of the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS), in co-sponsorship with the Human Learning and Behavior Branch, Center for Research for Mothers and Children of the National Institute of Child Health and Human Development (NICHD) encourages the submission of research grant applications (R01) on brain dysfunction in disorders of learning.

BACKGROUND

Learning disorders affect one of the largest groups of handicapped children as defined under Public Law 94-142. Estimates of incidence of unexpected school failure range from 2% to 20% of the school population. A major etiological hypothesis is the presence of subtle neurophysiological abnormalities in brain electrical activity of these children who show deficits in attention, memory, and control of motor activity, as well as in information processing. The Developmental Neurology Branch, Neurological Disorders Program (NINCDS) and the Human Learning and Behavior Branch, Center for Research for Mothers and Children (NICHD) encourage the submission of applications for the support of basic and clinical research on the neurophysiological and/or neurochemical mechanisms associated with specific and precisely defined learning disorders in children with normal intelligence, normal psychiatric status, and adequate environmental support. Similar studies of the same mechanisms in control children with normally developing cognition are also encouraged.

RESEARCH GOALS

Research grant applications should focus on brain neurophysiology and/or neurochemistry, but related research supporting this effort would be appropriate. Of particular interest are studies using evoked potential and EEG measures. Other areas of interest include neuroendocrine, metabolic and neuroradiological studies. The two primary research goals are: (1) to develop objective and reproducible diagnostic criteria for identifying homogeneous subgroups of children with learning disorders; (2) to refine neurophysiological techniques for evaluating cortical functions in these LD subgroups and in normal comparison groups. The reliability and validity of measures of brain electrical activity need to be investigated in both study and normal control groups by age, sex, type of learning task, and hemispheric specialization. Research should be directed at

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This program is described in the Catalog of Federal Domestic Assistance No. 13.852, Neurological Disorders, and 13.865, Research for Mothers and Children. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

developing knowledge of the neurophysiology of learning disorders, and expanding the capability for accurate diagnosis. This research would require a multidisciplinary approach involving participation from such areas as neurophysiology, developmental neuropsychology and pediatric neurology.

MECHANISM OF SUPPORT

Support for this program will be through the regular research project grant-in-aid. Each successful applicant will plan, direct, and carry out the individual research project.

APPLICATION AND REVIEW PROCEDURES

Applications should be prepared on Form PHS 398 (Revised 5/80) following instructions contained in the application kit. Application kits are available from most institutional business offices, or may be obtained from the Division of Research Grants, at the address given below.

Applications must be responsive to the program announcement and the goals of NINCDS and NICHD. They will be judged on scientific merit and program relevance in accordance with NIH policy and procedures involving peer review. An initial review will be made by the appropriate study section of the Division of Research Grants. A second level of review will be made by the National Advisory Neurological and Communicative Disorders and Stroke Council or by the National Advisory Child Health and Human Development Council depending on Institute assignment of the application.

Deadline dates for the receipt of applications are March 1, July 1, and November 1.

The phrase "Prepared in response to NINCDS and NICHD program announcement for research on brain dysfunction in disorders of learning" should be typed across the top of the first (face) page of the application. The original and six copies of the application should be mailed to:

Division of Research Grants
National Institutes of Health
Room 240, Westwood Building
5333 Westbard Avenue
Bethesda, Maryland 20205

One copy of the application is to be sent to each of the addresses below. Also, for further information applicants may contact:

Sarah H. Broman, Ph.D.
Acting Chief, Mental Retardation and Learning
  Disorders Section
Developmental Neurology Branch
Neurological Disorders Program
National Institute of Neurological and
  Communicative Disorders and Stroke
Federal Building, Room 8C-06
7550 Wisconsin Avenue
Bethesda, Maryland 20205
Telephone: (301) 496-6377

Norman A. Krasnegor, Ph.D.
Chief, Human Learning and Behavior Branch
Center for Research for Mothers and Children
National Institute for Child Health and
Human Development
Landow Building, Room 7C-18
7910 Woodmont Avenue
Bethesda, Maryland 20205
Telephone: (301) 496-6591

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

NIH-NHLBI-DLD-82G-B

SPECIALIZED CENTERS OF RESEARCH IN ADULT RESPIRATORY FAILURE

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

I. BACKGROUND

The Division of Lung Diseases of the National Heart, Lung, and Blood Institute invites new or competitive renewal applications for grants to support Specialized Centers of Research (SCOR) for basic and clinical investigations addressed to Adult Respiratory Failure. In addition to the Adult Respiratory Failure program, the Division currently supports SCOR programs in Chronic Obstructive Lung Diseases, Fibrotic and Immunologic Interstitial Lung Diseases, Pediatric Pulmonary Diseases, and Pulmonary Vascular Diseases.

This SCOR program complements other programs supported by the Division. It fosters a concerted research effort that involves basic disciplines but has a major emphasis on clinical problems relevant to the prevention, diagnosis, and management of adult respiratory failure. Special features of the SCOR grant are the following:

- It provides the opportunity for investigators with mutual or complementary interests to engage in interdisciplinary research focused on problems of adult respiratory failure as identified in this announcement.

- While clinical aspects of the disease must be the primary emphasis, the center program must include fundamental studies. The basic research must be clearly related to the disease focus, and must contribute, directly or indirectly, to the elucidation of mechanisms underlying the disease process, or to better diagnosis, management, or prevention of the disease. The SCOR grant may include projects designed to accelerate the transfer of knowledge gained from research to its use in medical practice.

- Each center must have a well-delineated organizational structure and administrative mechanism to ensure a productive research effort that will further the stated goals of the grant.

- Inherent in the SCOR program is the special interaction between all the centers, which is coordinated by the Division of Lung Diseases. The Division will provide advice and guidance to meet the goals of the Division's National Program as well as the goals of the SCOR grant. To these ends, the Division will provide, as part of the grant, funds specifically allocated for SCOR coordination. This makes it possible for investigators in different centers to

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This program is described in the Catalog of Federal Domestic Assistance No. 13.838, Lung Diseases. Grants will be awarded under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended: 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

meet and discuss problems of mutual interest and to engage in workshops addressed to specific facets of the SCOR program.

- The Division's SCOR program and each SCOR grant undergo periodic evaluation. Also, reports of progress are prepared for the information of the Pulmonary Diseases Advisory Committee and the National Heart, Lung and Blood Advisory Council.

Because of the size and complexity of a SCOR, prospective applicants are urged to take advantage of the opportunity to consult with the staff of the Division of Lung Diseases early in the preparation of the application (See Section V).

II. RESEARCH GOALS AND SCOPE

To be acceptable for the Adult Respiratory Failure SCOR competition, the focus of an application must be on adult respiratory distress syndrome that can be associated with such conditions as trauma, fat embolism, near-drowning, aspiration, drug overdose, sepsis, pneumonia, and other acute illnesses. The SCOR will not support investigations of acute respiratory failure that results from progression of such chronic pulmonary disorders as asthma, chronic bronchitis, or emphysema, in which prolonged pulmonary damage and respiratory insufficiency precede acute respiratory failure. This program also excludes neonatal respiratory distress syndrome.

The overall goal of the Division of Lung Diseases for the adult respiratory failure program is to improve the diagnosis, management, and prevention of the disease through the better understanding of the structural, biochemical, immunologic, and physiologic mechanisms and structural changes associated with acute lung injury. Therefore, a SCOR should be planned so the knowledge gained from fundamental investigations will be relevant to the clinical studies of the natural history of the disease, its diagnosis, treatment, and prevention.

The primary focus of the clinical and fundamental research projects that comprise the SCOR program should be the elucidation of the mechanisms of acute lung injury which result in adult respiratory failure, the mechanisms of lung repair, and the means by which therapeutic interventions can prevent progressive damage or accelerate repair processes.

A proposed SCOR may include pilot studies to test innovative approaches for diagnosis or therapy, but support will be provided only for the preliminary phases of such studies and not for large scale clinical evaluations. Costs for research patients may be charged only insofar as they result from the purely research aspects of care and if they clearly relate to the requirements of the proposed research.

To be responsive to this announcement, the proposed SCOR must include the following:

1. Clinical investigations addressed to the etiologies, natural history, diagnosis, treatment, or prevention of adult respiratory failure;*

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* A given SCOR need not address all of the above problems but must address some from both items 1 and 2.

2. Fundamental investigations of the mechanisms of acute lung injury, sites of damage, processes involved in progression and repair of the injury, or alterations in lung function associated with acute lung injury;*

3. A clinical core unit that will provide a patient population for the clinical studies; and

4. A well-delineated plan for a mutually supportive interaction between investigators involved in the clinical and the fundamental research aspects of the proposed SCOR.

III. MECHANISM OF SUPPORT

The support mechanism will be the grant-in-aid. Thus, all policies and requirements which govern the grant programs of the PHS will prevail, including the requirement for cost sharing. However, it will differ from other research grants in its degree of goal orientation and in the degree of direct participation by the National Heart, Lung and Blood Institute. While it is expected that the investigators of the individual SCORs will plan, direct, and execute their own research program, any substantive modifications in that program must be mutually agreed upon by the National Heart, Lung and Blood Institute. Ongoing evaluation will include periodic visits to the SCOR institutions and review of formal progress reports.

Applicants are requested to furnish their own estimates of the time required to achieve specific objectives of the proposed work, a schedule for completion of the work, or an outline of the phases or segments into which the proposed program can be logically divided. Awards will be for a maximum 5 year period; a December 1, 1983, start date should be requested.

Although this solicitation will be included and provided for in the fiscal plans for Fiscal Year 1984, support of grants pursuant to this request for applications is contingent upon receipt of appropriated funds for this purpose. The current Adult Respiratory Failure SCOR program involves three grants which have a total annual funding base of approximately two million dollars (including indirect costs). At this time, it is not possible to predict whether future funding will be above or below this level. The final allocation of funds to this program will be influenced by the total amount of funds available to the Division, by the overall merit of proposals, and by their relevance to the program goals. A variety of approaches would be responsive to this announcement; accordingly, it is anticipated that there will be a range of costs among individual grants awarded.

IV. REVIEW PROCEDURES AND CRITERIA

The merit review of these applications will be conducted by the National Heart, Lung, and Blood Institute. Primary review will be conducted by a group of consultants specifically convened for this purpose. Secondary review will be by the National Heart, Lung and Blood Advisory Council. Applicants will be informed of the results of the competition as soon as possible after the May 1983 meeting of the Council.

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* A given SCOR need not address all of the above problems but must address some from both items 1 and 2.

The review criteria include:

- The scientific merit of each research project and the relation of the project to the overall goals of the center;
- The technical merit and justification of each core unit;
- The accomplishments and progress to date, particularly for renewal applications;
- The qualifications, experience, and commitment of the investigators responsible for the research projects or core units and their ability to devote adequate time and effort to the program; and
- The appropriateness of the budget for the proposed projects and core units.

REVIEW OF THE CENTER AS AN INTEGRATED EFFORT

The review criteria include:

- The significance and the importance of the research to the programmatic goals of the SCOR announcement;
- The multidisciplinary scope of the center and the coordination and interrelation of the research projects and core units;
- The leadership and scientific stature of the program director and his or her commitment and ability to devote adequate time and effort to the program;
- The participation of an effective number of responsible experienced investigators;
- The academic and physical environment in which the research would be conducted, including the availability of space, equipment, patients, and the potential for interaction with scientists from other departments and other institutions;
- The internal arrangement for quality control of on-going research, the allocation of funds, day-to-day management, communication and cooperation between the investigators involved in the program, and contractual agreements;
- The presence of an administrative and organizational structure that would facilitate attainment of the proposed objective of the program;
- The institutional commitment to the requirements of the program; and
- The appropriateness of the budget to the proposed program.

REVIEW OF THE PROPOSED CENTER BY THE NATIONAL HEART, LUNG, AND BLOOD ADVISORY COUNCIL

Factors considered in this review include:

- The results of the initial review for scientific and technical merit;
- The significance of the research program to the adult respiratory failure program;
- National needs; and
- Policy and budgetary consideration.

V. METHOD OF APPLYING

SPECIFIC GUIDELINES FOR PREPARATION OF AN APPLICATION FOR A SPECIALIZED CENTER OF RESEARCH ARE AVAILABLE UPON REQUEST. PROSPECTIVE APPLICANTS ARE URGED TO WRITE FOR THESE GUIDELINES EARLY IN THE PLANNING STAGE.

To the extent possible, the Division of Lung Diseases is prepared to discuss plans for developing a SCOR proposal with prospective applicants. However, to provide effective guidance, the Division must receive a draft that is complete with regard to all substantive sections. These include description of SCOR goals, detailed presentations of projects and cores, description of organization and administrative plans, detailed budgets for each project and core and biographical data for all participating investigators.

Inquiries about preparation of applications should be addressed to:

Carol E. Vreim, Ph.D.
Chief, Interstitial Lung Diseases Branch
Division of Lung Diseases
National Heart, Lung, and Blood Institute
Westwood Building, Room 6A05
5333 Westbard Avenue
Bethesda, Maryland 20205

Telephone: (301) 496-7034

To provide an estimate of the nunmber of applications, for purposes of planning the review, prospective applicants should submit a brief letter of intent (not to exceed two pages) no later than July 1, 1982, describing the proposed goals of the SCOR, types of projects to be included, names of responsible investigators with academic titles, and an estimate of the level of funding (direct costs) required. Letters of intent are not binding.

Letters of intent should be sent to:

Charles Turbyfill, Ph.D.
Chief, Centers and Special Projects Review Section
Division of Extramural Affairs
National Heart, Lung, and Blood Institute
Westwood Building, Room 553A
5333 Westbard Avenue
Bethesda, Maryland 20205

Application form PHS 398 should be used. Forms may be obtained from the institution's application control office or from the Division of Research Grants, NIH.

The completed application and 24 copies should be delivered to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205

Two additional copies should be mailed to the Division of Lung Diseases, NIH.

Applications must be received by September 15, 1982.

A brief covering letter should accompany the application indicating that the proposal is being submitted in response to this Request for Applications NHLBI-DLD-82G-B.

Consequences of Lack of Responsiveness to the RFA or Late Submission

Applications submitted in response to this request will be reviewed by NHLBI staff to determine responsiveness to the criteria for a Specialized Center of Research. Those applications that are judged not responsive, or are not received by September 15, 1982, will not be accepted for review and will be returned to the applicant.

Timetable

Letters of intent should be submitted no later than July 1, 1982.

The original and 24 copies of the completed application should be submitted to the Division of Reserch Grants, NIH not later than September 15, 1982. Two additional copies should be submitted to the Division of Lung Diseases.

The final review of applications by the National Heart, Lung, and Blood Advisory Council will be completed by May 28, 1983.

Applicants will be notified of the outcome of the review by June 1983.

Initiation of awards will not be before December 1, 1983.

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

RFA-NHLBI-DLD-82G-C

STRUCTURAL AND FUNCTIONAL CHANGES ASSOCIATED WITH RESPIRATORY MUSCLE FATIGUE

NATIONAL HEART, LUNG AND BLOOD INSTITUTE

I. BACKGROUND

Although fatigue of respiratory muscles has long been thought to contribute to respiratory failure, the extent to which ventilatory muscle fatigue is involved in respiratory disability and failure is still not well-documented. Nevertheless, it appears likely that when the mechanisms involved in such fatigue are more thoroughly understood, effective means for detection, prevention, and treatment of fatigue may be identified and significant improvements made in the care and treatment of persons with a variety of lung disorders.

The most direct definition for ventilatory muscle fatigue is failure of task performance. Inability to continue voluntary hyperpnea at a specified level, to tolerate inspiratory resistive loading, or to generate specific pressures at the airway or across the diaphragm during resistive loading have served as criteria for ventilatory muscle fatigue. Accompanying the development of fatigue is a shift in the electromyogram (EMG) power spectrum (the distribution of power versus frequency). Finally, changes in respiratory patterns are seen in circumstances associated with fatigue or with EMG changes.

The exact physiological, morphological, and biochemical causes of fatigue in respiratory muscles, and the changes associated with fatigue, have not been explored. Although our understanding of skeletal muscle fatigue has progressed considerably over the past decade, largely through the study of isolated limb muscles, the respiratory system has several features that make it difficult to extrapolate this knowledge to the respiratory muscles. First, the activation of the muscles is under both voluntary and involuntary control, and knowledge about neural control of breathing during fatigue is at best very limited. Second, the diaphragm, the principal muscle of respiration, receives its blood supply largely over the surface of the muscle rather than through the muscle mass itself and thus is less liable to interruptions in the supply of oxygen and nutrients during a contraction. The biochemistry of diaphragmatic fatigue and its responsiveness to pharmacologic therapy may therefor be different from fatigue in other muscles. Third, the diaphragm is aided in its function by intercostal and accessory muscles that may, as the diaphragm reaches its limits of endurance, take on some or all of the burden of ventilation, thus "resting" the diaphragm and postponing the advent of ventilatory failure. The ability of the accessory muscles to cope with such demands and the neural mechanisms involved in such a shift of muscular activation have received little attention.

This program is described in the Catalog of Federal Domestic Assistance, No. 13.838, Lung Diseases. Grants will be awarded under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended: 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

II. GOALS AND SCOPE

The specific goal of this program is to encourage collaboration between researchers in different disciplines and fields for the purpose of elucidating basic mechanisms of respiratory muscle fatigue. Thus, to be responsive to this RFA, interdisciplinary efforts (such as between researchers in the disciplines of physiology, biochemistry or morphology) or intradisciplinary approaches (such as between neuro- and respiratory physiologists) are required. The studies should be based on common goals and must be designed to test a specific hypothesis or a few closely related hypotheses.

Physiological as well as biochemical, morphologic, and neurologic aspects of fatigue in the normal respiratory system, the influence of various lung diseases and associated changes in lung and chest wall mechanics on muscle fatigue, and the neural control of breathing during fatigue are examples of areas of research that will be supported under this announcement. Studies may include whole animal or isolated muscle preparations. If the latter are used, care should be taken to ensure that the studies are relevant to an in vivo situation. Although it is expected that proposals will be primarily addressed to animal studies, human studies may also be included if clearly related to elucidation of basic mechanisms of fatigue. Basic research, such as investigations of lung and chest wall mechanics or central and peripheral neural control and transmission, may be proposed if the intent is to correlate the studies with an understanding of fatigue mechanisms, but the major emphasis must be on the latter.

Although the importance of overall nutritional status on respiratory muscle structure and function is recognized, studies dealing with whole body nutrition as an independent variable will not be considered responsive to this announcement. In addition, methodological studies aimed at developing or improving clinical means of detection of respiratory muscle fatigue, and clinical studies on prevention (e.g., respiratory muscle training) and treatment (e.g., optimal use of ventilators, drugs, etc., in cases where fatigue has resulted in the patient's inability to maintain adequate gas exchange) of respiratory muscle fatigue, while of importance, will not be supported by this RFA.

III. EXAMPLES OF RESEARCH TOPICS

The research topics presented below serve as examples of research areas that would meet the goals of this program. The topics mentioned are not intended to be all inclusive and are not presented in any order of priority. Investigators are encouraged to consider other relevant topics and approaches that would lead to an understanding of respiratory muscle fatigue.

With other skeletal muscles, it has been demonstrated that fatigue can be the result of a failure at one of several sites. Central fatigue would be characterized by a failure of the central nervous system to provide sufficient neural stimuli to maintain the required muscle output. Fatigue can occur due to depletion of neuro-transmitters, either at a ganglionic site or at the neuromuscular junction. Finally, numerous biochemical disturbances, such as inadequate supply of energy-producing substrates or the accumulation of wastes, can result in a failure of contraction at the cellular level. Few studies have been done to identify the critical site(s) of fatigue in respiratory muscles. These have dealt with a few aspects of diaphragmatic metabolism, but have not identified a specific metabolite or metabolic pathway that may be considered rate limiting and therefore a cause of fatigue. It is important to identify which link in the muscle activation pathway may be the weakest and under what conditions it or a different link may be expected to fail.

Much has been learned about the role of the "accessory" muscles of respiration during normal (non-fatigued) breathing. The intercostals and abdominal muscles are activated even at rest during inspiration to stiffen the rib cage and to keep the diaphragm at a more nearly optimal length. During exercise, other accessory muscles are activated to help the diaphragm with the increased load. Little is known, however, about the mechanics of the lung and chest wall during progressive fatigue. Discoordinate rib cage and abdominal motion has been observed, but the muscles involved, their fatigue limits, and the pressures that they generate require further study. In addition, such basic characteristics of respiratory muscle function as force-velocity and force-length responses under, for example, various regimens of stimulation, alterations of nutrient supply, or disease states, are not well known and require further study.

Diseases affecting lung function are known to have an effect on respiratory muscle structure and function. For instance, the diaphragm is known to operate at a shorter, less efficient length in patients suffering from emphysema when lung hyperinflation is present. Such patients, if adequately nourished, have been found at autopsy to have diaphragms that are thicker than those of people with normal lungs; this thickening may help compensate for the disadvantage of operating at a shorter length. The morphology and fatigue characteristics of such diaphragms need to be understood more completely. Similar fatigue studies are also required in neonates who have immature respiratory systems as well as in patients with altered lung mechanics due to fibrotic diseases or asthma. Even the oxygen cost of breathing and changes in efficiency of the respiratory muscles are not well described in many disease states including respiratory failure. Thus, animal studies involving immature lungs or lungs with experimentally induced and well characterized changes in lung elastic or resistive properties should yield useful data on respiratory muscle fatigue.

IV. MECHANISM OF SUPPORT

The support mechanism for this program will be the regular NIH grant-in-aid; successful applicants will plan and execute their own research program. Upon initiation of the program, the Division of Lung Diseases will sponsor periodic workshops to encourage exchange of information among investigators who participate in this program. Prospective grantees should include in their grant applications a statement indicating their willingness to participate in such information exchange activities.

Although this program is included in the financial plans for Fiscal 1982, award of grants pursuant to this request for grant applications is contingent upon receipt of appropriated funds for this purpose. It is anticipated that four to six proposals will be supported under this program. Since a variety of approaches would represent valid responses to this announcement, it is anticipated that there will be a range of costs among individual grants awarded. Although interdisciplinary approaches are encouraged, grant applications should be tightly focused; it is not the intent of this request to solicit proposals for large multidisciplinary studies (program projects) encompassing a variety of essentially independent research projects. Applicants are requested to furnish their own estimates of the time required to achieve the objectives of the proposed research project; however, the award period for this proposal must not exceed 3 years. At the end of the initial award period, renewal proposals may be submitted for further competitive review through the regular grant mechanism. It is anticipated that support will begin on September 30, 1982.

The current policies and requirements which govern the research grant programs of the National Institutes of Health will prevail, including the requirement for cost sharing.

V. REVIEW PROCEDURES AND CRITERIA

Upon receipt, applications will be reviewed for their responsiveness to the specific objectives described in this announcement. If an application is judged unresponsive, the applicant will be contacted and given an opportunity to withdraw the application or to submit it for consideration in the traditional grant program of the NIH. Initial technical merit review will be arranged by the Division of Research Grants (DRG). Secondary review will be undertaken by the National Heart, Lung, and Blood Advisory Council.

If a proposal submitted in response to this RFA is identical to a research grant application already submitted to the NIH for review, the applicant will be asked to withdraw the pending application before the new one is accepted. Simultaneous submission of identical applications will not be allowed.

The factors to be considered in the scientific merit evaluation of each application will be identical to those used in traditional NIH research grant application evaluation, including an assessment of the importance of the proposed research problem; the novelty and originality of the approach; the training, experience, and research competence or promise of the investigator(s); the adequacy of the experimental design; the suitability of the facilities; and the appropriateness of the requested budget to the work proposed.

VI. METHOD OF APPLYING

1. Letter of Intent

Prospective applicants are asked to submit a brief letter of intent which would include a synopsis of the proposed research as well as the names of other institutions which might collaborate on the project. Such letters are requested only to obtain an indication of the number and scope of applications to be received. A letter of intent is not a requirement for application, nor is it binding, and information provided in the letter will not enter into the review of any application subsequently submitted.

The letter of intent should be received by February 15, 1982, addressed to Dr. Everett E. Sinnett, Division of Lung Diseases, NHLBI, National Institutes of Health, Westwood Building, Room 6A03, Bethesda, Maryland 20205.

2. Format for Applications

Applications should be submitted on the standard research grant application form, PHS-398 (Revised 5/80), which may be obtained at the applicant's institution business or research office or by contacting the Division of Research Grants, Office of Grants Inquiries, Room 449, Westwood Building, Bethesda, Maryland 20205, phone (301) 496-7591. The conventional presentation in format and detail for regular research grant applications should be utilized.

3. Application Procedure

The completed application and 24 copies should be sent or delivered to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205

To ensure their review, applications must be received by April 15, 1982.

The face page of the application must indicate that it is submitted in response to this program announcement: RFA-NHLBI-DLD-82G-C, "Structural and Functional Changes Associated with Respiratory Muscle Fatigue."

4. Timetable

Letter of Intent due	February 15, 1982
Applications to Division of Research Grants due	April 15, 1982
NHLB Advisory Council Review	September, 1982
Initiation of awards not before	September 30, 1982

VII. INQUIRIES

Inquiries may be directed to Dr. Everett E. Sinnett, Division of Lung Diseases, NHLBI, National Institutes of Health, Westwood Building, Room 6A03, Bethesda, Maryland 20205. Telephone: (301) 496-7171.

REQUEST FOR RESEARCH GRANT APPLICATION: RFA NIH-NHLBI-82G-E

IDENTIFICATION OF CELLS IN ATHEROSCLEROTIC PLAQUES

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Application receipt date: April 1, 1982

The National Heart, Lung, and Blood Institute (NHLBI) invites applications for research grants, to be initiated during FY 1982, to develop and apply improved methods, particularly biochemical and marker methods, which in conjunction with morphology can 1) improve the accuracy and ease of identification of normal and abnormal cells in atherosclerotic plaques, and 2) assess the specific characteristics of cells at various stages of plaque development. The present RFA is for a single competition, with the deadline specified above..

BACKGROUND INFORMATION

For many decades attempts have been made to identify the changes in the arterial wall and the cells involved in the development of atherosclerotic lesions. It is not always possible to identify different types of cells with certainty. There is a great deal of variation among lesions including both the kinds and proportions of cells present and the particular stages of cellular differentiation that may be found. A detailed and accurate appreciation of the identity and range of phenotypic characteristics of such cells should greatly enhance our understanding of the pathogenesis of atherosclerotic plaques.

Study of the role of vascular cells in atherogenesis has suggested that atherosclerosis may involve the reaction of the vessel wall to cycles of injury-repair in which monocytes, leukocytes, platelets, macrophages, smooth muscle cells, fibroblasts and endothelial cells play a part.

RESEARCH GOALS AND SCOPE

The cells associated with atherosclerotic plaques have been designated in many ways. Some are designated according to cell type, others by purely descriptive terms without assignment to a cell type or origin although particular properties and characteristics may be described. Normally differentiated cells are easily recognized, but differentiation is commonly unusual and recognition of cell types is often difficult or impossible. The goal of this RFA is to elicit applications which hold substantial promise of significantly advancing the state of the art for one or more aspects of the identification of cell types, detection and quantification of their biochemical activity and functions in different stages of differentiation and in different kinds of plaques.

This program is described in the Catalog of Federal Domestic Assistance, number 13.837, Heart and Vascular Diseases Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency Review.

There is the possibility of improving methods and markers, or finding new markers to identify properties and characteristics of cells in or derived from plaque. Some of these technical improvements relate to biochemical, immunological or physical methods, some can assess function, and all can be associated with morphology. However, this RFA is not directed to research that is primarily morphological. While the ultimate interest is in human atherosclerosis, animal lesions and cell culture models can provide valuable information.

MECHANISM OF SUPPORT

The support mechanism for this program will be the NIH research project grant. This type of announcement (the RFA) is used when the Institute--with the concurrence of its National Advisory Council--wishes to stimulate investigator interest in a particular research problem that is important to its program.

The RFA identifies the scope of the Institute's interest but does not require that the application to be submitted conform to a specific protocol. Thus it is expected that each successful applicant will plan, direct, and carry out his or her research proposal within the general scope or frame of reference. As with any research grant, the recipient must obtain prior approval for any major change in the scope or objectives of the approved project. Applicants should be aware that the general requirement is particularly pertinent when, as in the case of RFA solicitations, the awarding Institute has committed funds in response to a specific program need.

Applicants are requested to furnish their own estimates of the time required to achieve the specific objectives of the proposed work, but the total project period should not exceed three years in duration; a September 30, 1982 start date should be requested.

REVIEW PROCEDURES AND CRITERIA

Applications will be reviewed in a national competition with one another. Primary review will be conducted by an Initial Review Group composed in the main of non-Federal scientific consultants. Secondary review will be by the National Heart, Lung, and Blood Advisory Council. Applicants will be informed of the results of the competition as soon as possible after the September 1982 meeting of the Council.

The major factors to be considered in evaluating each application are given below:

- The relevance and significance of the proposed approach to the goals described in this announcement.
- The scientific merit of the proposal: the methodology, the research design, the plan for analysis and interpretation of data.
- The research experience and competence of the applicant(s) to carry out the proposed investigations.
- Adequacy of time/effort to be devoted to the project by investigators and technical staff.
- Adequacy of collaborative arrangement(s) if applicable.
- Adequacy of facilities and resources for the proposed research.
- Justification for the proposed budget in relation to the scope of the project.

METHOD OF APPLYING

A. LETTER OF INTENT

Prospective applicants are asked to submit a brief, one-page letter of intent which includes a very brief synopsis of the proposed areas of research to

Dr. Charles Turbyfill
Division of Extramural Affairs
National Heart, Lung, and Blood Institute
5333 Westbard Avenue
Bethesda, MD 20205

This letter should be received no later than February 15, 1982.

The Institute requests such letters for the purpose of providing an indication of the number and scope of applications to be received. A letter of intent is not binding, and it will not enter into the review of any application subsequently submitted, nor is it a necessary requirement for application.

B. FORMAT FOR APPLICATION

Applications should be submitted on form PHS 398, the application form for a regular research grant. This form is available at the applicant's institutional office of sponsored research or from the Office of Grants Inquiries, Division of Research Grants, NIH. The conventional format of research grant applications should be utilized ensuring that the points identified under "Review Procedures and Criteria" are addressed.

C. APPLICATION PROCEDURE

The completed application and thirty (30) copies thereof should be sent or delivered to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205

To ensure their review, applications must be received by April 1, 1982. Applications not received by this deadline will be considered ineligible for this competition but after discussion with the applicant, may be considered as a regular research grant application which meets the usual July 1, 1982 deadline. If an application is judged to be non-responsive to this announcement, the applicant will be contacted to determine if he or she wishes to have the proposal returned or reviewed as an application for a regular research grant. Due dates are as follows:

Letter of Intent	February 15, 1982
Application Due	April 1, 1982
Grant Start Date	September 30, 1982

PLEASE NOTE
The outside of the mailing package and the top of the face page of the application should be labeled: "Response to RFA NIH-NHLBI-82G-E"

FUNDING

Although this program is included and provided for in the Institute's financial plans for FY 1982, awards are contingent upon ultimate allocation of appropriated funds for this purpose. It is expected that up to $700,000 for total costs will be available for the first year to support approximately five grant awards.

IDENTIFICATION OF CONTACT POINTS

Inquiries may be directed to Dr. Edwin C. Gangloff, Division of Heart and Vascular Diseases, National Heart, Lung, and Blood Institute, Federal Building, Room 4C-12, Bethesda, Maryland 20205; Telephone (301) 496-1978.

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

RFA-NIH-NHLBI-82G-F

ANALYSIS OF THE ROLE OF GENETIC AND DEVELOPMENTAL FACTORS IN THE ETIOLOGY AND PROGRESSION OF ESSENTIAL HYPERTENSION

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Application receipt date: April 1, 1982

The National Heart, Lung, and Blood Institute (NHLBI) invites applications for grants from interested investigators for studies on the role of genetic and developmental factors in the etiology and progression of essential hypertension. The proposed studies would seek, as their major objective, to investigate the effects of genetic, prenatal and/or postnatal factors on the development of "essential hypertension" through the use of animal models.

Grants are awarded only to nonprofit organizations and institutions, governments and their agencies, and occasionally to individuals. This type of grant solicitation (the RFA) is utilized when it is desired to encourage investigator-initiated research projects in areas of special importance to the National Heart and Vascular Disease Research Program. Applicants funded under the RFA are supported through the customary NIH grant-in-aid, in accordance with PHS policies applicable to Research Project Grants, including cost sharing. However, the RFA solicitation represents a single competition, with a specified deadline for receipt of applications. All applications received in response to the RFA will be reviewed by the same National Institutes of Health (NIH) Initial Review Group.

It is important to call attention to the fact that the RFA application differs from that for the regular research grant in that it is requested that a letter of intent to submit an application be sent by February 15, 1982, and that the applications be received by the April 1, 1982 deadline. More detailed instructions are provided under Section V, Method of Applying.

I. BACKGROUND INFORMATION

A. The Behavioral Medicine Program

As a component of the Clinical Application and Prevention Program of the Division of Heart and Vascular Diseases, the Behavioral Medicine Branch is responsible for support of biobehavioral research activities related to cardiovascular health and disease issues. To this end, the branch seeks to foster collaboration between the biomedical and behavioral science communities on research problems of mutual concern. The scope of the research supported by the branch extends from basic studies on central nervous system - cardiovascular system interaction to health

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This program is described in the Catalog of Federal Domestic Assistance No. 13.837, Heart and Vascular Disease Research. Awards will be made under the authority of the Public Health Service Act, Section 301 (42 USC 241) and administered under PHS grant policies and Federal Regulations, most specifically 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

promotion/disease prevention issues. Focusing on basic research using animal models, the investigations to be supported through this RFA are intended as a primary step in identifying the separate as well as the interactive contributions of genetic and early environmental factors to the development of essential hypertension.

B. Historical Perspective

Hypertension has been brought to the forefront of medical attention by recent studies; the benefits derived from eliminating even mildly increased blood pressures in humans have been demonstrated. Efforts to prevent and treat hypertension, however, have been hampered by a lack of knowledge concerning its etiology. Genetic, dietary, environmental and psychological factors have all been implicated. Epidemiological studies in human populations have demonstrated familial aggregation of hypertension, differences in blood pressure based on dietary practices, and in fact, have implicated both heredity and environment as causal factors for development of hypertension.

Systematic studies of the effects of heredity and environment have been lacking, although there have been notable successes with animal models in selective breeding for hypertension. These efforts have resulted in strains of animals which show marked propensity to develop hypertension spontaneously or under dietary (salt) stress.

The roles of the intrauterine environment, maternal behavior and heredity have not been systematically investigated to determine their relative contributions to the development of essential hypertension. Eating habits, dietary preference, activity, sensitivity to psychological stress, and autonomic responsivity all appear to play some part in this process. Techniques are now available to identify, describe and quantify the relative roles of genetic, intrauterine and maternal factors in the development of neural, cardiovascular and behavioral dysfunctions that could produce high blood pressure.

II. RESEARCH GOALS AND SCOPE

Investigation of the roles of genetic and developmental factors is thus appropriate, using animal models as a basis for understanding possible parallel contributions of genetic or environmental factors in essential hypertension in humans. For illustrative purposes, some general areas of relevant research effort are listed below. Other areas or methodologies may occur to the applicant which would be appropriate to the objectives. New concepts and approaches are encouraged. In all instances, the perceived relationship and importance of the proposed work to the improved understanding of genetic and developmental factors in hypertension should be made explicit.

Embryo transplantation and cross fostering between genetically selected strains of animals are among the techniques that could provide the methodological basis for such proposals. A genetically homogeneous strain of animals predisposed to hypertension can provide the embryos to be transplanted into a normal strain and vice versa. Offspring can either remain with the mother who has carried and delivered them or can be cross fostered to another mother of a similar or dissimilar strain. Physical, psychological, and physiological stressors can be introduced at various stages of embryonic developmenmt. By combining these approaches, the contribution of heredity, maternal behavior and intrauterine environment to the subsequent development of hypertension can be described.

Such a systematic approach can provide the basis for a series of investigations oriented toward the elucidation of the various risk factors for the development of hypertension. Examples of risk factors which may be investigated include, but are not limited to, dietary preferences, exercise, sodium intake, increased susceptibility and cardiovascular responsivity to psychological stress, or alterations in renal blood flow and subsequent hormonal activity in response to stress.

Applications should identify the hypothesis and clearly outline the questions proposed for investigation. The description of the proposed studies should include the research design and methodology, including procedures for the analysis and interpretation of data.

Potential applicants should review their research proposals in the context of the enunciated program goals and review criteria to reassure themselves that their application is truly responsive; if the relevance and responsiveness of a research proposal to these goals and criteria are tenuous, the application should be considered for submission as a regular research grant application. It should be recognized that the existence of a targeted program and the distribution of a request for grant applications does not preempt the topic from the regular research grant program.

Because this program is one in which the various elements have relevance to one another and may depend upon each other, free communication is expected between the participants. In the preparation of the budget for the grant application, applicants should request travel funds for one, two-day research conference each year, most likely to be held in Bethesda, Maryland.

III. MECHANISMS OF SUPPORT

The support mechanism for this program will be the NIH research project grant. This type of announcement (the RFA) is used when the Institute--with the concurrence of its National Advisory Council--wishes to stimulate investigator interest in a particular research problem that is important to its program. The RFA solicitation represents a single competition with one specified deadline for receipt of application. All applications in response to an RFA are reviewed by the same initial review group usually for a designated amount of funds or number of awards.

The RFA identifies the scope of the Institute's interest but does not require that the proposal conform to a specific protocol. Thus it is expected that each successful applicant will plan, direct, and carry out the research program. As with any research grant, the recipient must obtain prior approval for any major change in the scope or objectives of the approved project. Applicants should be aware that this general requirement is particularly pertinent when, as in the case of RFA solicitations, the awarding Institute has committed funds in response to a special program need.

Applicants are requested to furnish their own estimates of the time required to achieve specific objectives of the proposed work and an outline of the phases or segments into which the proposed project can be logically divided. The total project period should not exceed three years in duration; a September 30, 1982 starting date for the project should be requested.

Although this announcement is included and provided for in the financial plans for Fiscal Year 1982, support of grants pursuant to this Request for Applications is contingent upon ultimate receipt of appropriated funds for this purpose. The total annual funding level for the program is estimated at $300,000. A variety of approaches would be responsive to this solicitation; accordingly, it is anticipated that there will be a range of costs among the individual grants awarded. It is anticipated that 5 to 6 awards will be made if a sufficient number of high quality applications is received; this should be considered in the preparation of the scope of work and budget.

Unless specifically stated to the contrary herein, all policies and requirements which govern the grant program of the PHS apply, including the requirement for cost sharing.

IV. REVIEW PROCEDURES AND CRITERIA

Applications will be reviewed in a national competition with each other. Primary review will be conducted by an Initial Review Group composed primarily of non-Federal scientific consultants. Secondary review will be by the National Heart, Lung, and Blood Advisory Council. Applicants will be informed of the results of the competition as soon as possible after the September, 1982 meeting of the Council.

The major factors considered in evaluating each applications will be:

1. The scientific merit of the application, that is, the questions proposed for study, the research design and approaches, the methodology, and the analysis and interpretation of data.

2. The likelihood of arriving at meaningful and useful data to accomplish the goal of this solicitation.

3. The research experience and competence of the staff to carry out the proposed investigations and the time they will devote to the program.

4. The adequacy of existing and proposed facilities and resources.

5. The organizational and administrative structure of the proposed program.

6. The evidence of institutional commitment to the program.

7. The cost of the proposed research.

V. METHOD OF APPLYING

A. Letter of Intent

Prospective applicants are asked to submit a brief, one-page letter of intent which includes a very brief synopsis of the proposed areas of research and identification of any other participating institutions. This letter should be sent no later than February 15, 1982 to:

Dr. Charles L. Turbyfill
Review Branch
Division of Extramural Affairs
National Heart, Lung, and Blood Institute
National Institutes of Health
Westwood Building, Room 553
5333 Westbard Avenue
Bethesda, MD 20205

The Institute requests such letters for the sole purpose of providing an indication of the number and scope of applications to be received. A letter of intent is not binding, and it will not enter into the review of any application subsequently submitted, nor is it a necessary requirement for application.

B. Format for Applications

Applications should be submitted on form PHS 398, the application form for a regular research grant. This form is available at the applicant's institutional control office or from the Division of Research Grants, NIH. The conventional format of research grant applications should be utilized, ensuring that the points identified under "Review Procedures and Criteria" (see Section IV above) are fulfilled. Specific attention is directed towards the inclusion of a statement indicating the willingness of the applicant to work cooperatively with other participants in the program and with the National Heart, Lung, and Blood Institute.

C. Application Procedure

The completed application ans six (6) copies should be sent or delivered to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
5333 Westbard Avenue
Bethesda, MD 20205

An additional twenty (20) copies of the application should be sent or delivered to:

Processing Section
Review Branch, Division of Extramural Affairs
National Heart, Lung, and Blood Institute
Westwood Building, Room 5A15
5333 Westbard Avenue
Bethesda, MD 20205

To ensure their review, applications must be received by April 1, 1982. Applications not received by this deadline will be considered ineligible and, after discussion with the applicant, may be considered as a regular research grant application. Concerning applications that are determined to be nonresponsive to this announcement, applicants will be contacted to determine if they wish to have the proposal returned or reviewed as a regular research grant.

The outside of the mailing package and the top of the face page of the applications should be labeled "Response to RFA NIH-NHLBI-DHVD-82G-F."

Applications will be accepted and reviewed as follows:

Application Receipt	Initial Review	Council Review	Start Date
April 1	June	September	September 30

VI. IDENTIFICATION OF CONTACT POINTS

Inquiries may be directed to:

Dr. Sonja B. Haber
Behavioral Medicine Branch
Division of Heart and Vascular Diseases
National Heart, Lung, and Blood Institute
Federal Building, Room 604
Bethesda, Maryland 20205

Telephone: (301) 496-9380

REQUEST FOR RESEARCH GRANT APPLICATION: RFA

RFA-NIH-NHLBI-DHVD-82G-H

MECHANISMS OF CALCIFICATION OF PROSTHETIC MATERIALS IN THE CARDIOVASCULAR SYSTEM

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Application receipt date: April 15, 1982

The Division of Heart and Vascular Diseases of the National Heart, Lung, and Blood Institute invites grant applications for research leading to a better understanding of the mechanisms of calcification of implanted cardiovascular prostheses.

Calcification of tissue valves in humans impairs their performance and thereby necessitates their replacement; this problem occurs more frequently in children than in adults. Calcification of the flexing elastomeric surfaces of implanted circulatory support devices is a frequent occurrence in calves and often necessitates termination of the experiment. The events which initiate this calcification process are unknown. The purpose of this special program is to stimulate research in this area. It is anticipated that a variety of approaches and expertise could be brought to bear on the solution of this problem. Among the disciplines and expertise which may be appropriate are calcium metabolism, immunology, hematology, pathology, surgery, veterinary medicine, and the physical, chemical and engineering sciences.

The Institute will use the grant-in-aid as the support mechanism, but it will differ from other research grants both in its goal orientation and in the expectation that grantees will exchange information and develop collaborations related to the research supported by this program. The present announcement is for a single competition with a specified deadline of April 15, 1982 for receipt of applications. It is open to all interested investigators, including those who are already the recipients of research grants from the NHLBI. Applications should be prepared and submitted in accordance with the aim and requirements described in the following sections.

I. BACKGROUND

A. The Biomaterials Program

The Division of Heart and Vascular Diseases of the National Heart, Lung, and Blood Institute has the responsibility to support research which leads to the design or improvement of prosthetic devices for the cardiovascular system. Within this framework, the biomaterials program supports research and development of biocompatible materials suitable for cardiovascular prostheses. Such cardiovascular prostheses may either support or replace a portion of the host

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This program is described in the Catalog of Federal Domestic Assistance, Number 13.837, Heart and Vascular Diseases Research. Awards will be made under the authority of the Public Health Service Act, Section 301 (42 USC 241) and administered under PHS grant policies and Federal Regulations, most specifically 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse of Health Systems Agency Review.

system which does not function adequately to meet physiologic needs. Basic and applied research in the design and function of heart valves, vascular grafts, intra-aortic balloons, ventricular assist devices and the total artificial heart has been supported through grant and contract programs of the Division of Heart and Vascular Diseases, particularly through the Devices and Technology Branch.

B. Historical Perspective

In the last decade, more than 60,000 xenograft valves have been implanted in adults and children. Recent data indicate that these valves may calcify at a greater rate than natural valves, particularly in the juvenile population. At the same time, it has been noted in experimental systems in calves that not only xenograft valves, but also the elastomeric flexing surfaces of circulatory support devices calcify within a period of a few months. Calcification of other types of cardiovascular prostheses has also been noted, including vascular grafts and materials in the perivascular space. In these situations, the consequences may be impaired physiologic function, failure of the prosthesis, and difficult surgical access when reoperation is required.

On the one hand, calcification is impairing clinical status of valve recipients and on the other it affects experimental progress. The relationship of these two situations is unknown, but is presumed to be related to similar underlying mechanisms. At the moment, there are only a few research studies devoted specifically to unravelling the mechanism and etiology of this process. Since the problem could have a serious impact on clinical care of heart valve recipients and could potentially limit the longevity of circulatory assist devices, additional effort to delineate the mechanisms of the process is necessary.

II. RESEARCH GOALS AND SCOPE

The proposed research should address the evaluation of a hypothesis concerning the mechanism of calcification of cardiovascular prostheses. The test system might be *in vitro* or *in vivo*; the role of blood or materials, or both, might be investigated. *Ideally*, the proposed hypothesis should be tested in a system in which the proposed variable can be manipulated independently and its change can be documented in order to test and verify the hypothesis. Clinical or experimental prosthetic devices may be used or, with adequate justification, an appropriate test configuration may be used. However, it is outside the scope of this RFA to support work for extensive development of new devices.

The role of circulating blood components in initiating or exacerbating the calcification process remains to be defined. Blood proteins, lipoproteins, or cells may contribute to the process, as well as inorganic ions, such as calcium and phosphate. It appears that calcification is related to blood-materials interactions and there is an assumption that it may be a consequence of thrombotic events. Studies which would define such relationships are within the scope of this RFA.

Calcification appears to be most severe on flexing surfaces of cardiovascular devices and therefore may be related to mechanical strain and/or stress. At flexing sites with a strain greater than 20%, injury to either the prosthetic surface or the absorbed biological layer has been noted at sites of frank calcification. The relationship of calcification to stress or the rate of stress/strain development has not been determined. Other factors which can be controlled in the prosthetic design, such as micro- and macro-flow profiles, bulk properties, surface chemistry or morphology have not been evaluated for possible contribution to the initiation of calcification of tissue or synthetic materials. Studies of such factors are appropriate to this RFA.

For an in vivo experiment, the species and age of the animal model should be clearly specified and justified. The appropriate animal model to predict long-term performance of cardiac devices in adults and children remains to be identified.

Calcification of biological or synthetic cardiovascular prostheses was not recognized as a problem until after extensive experience in humans or long-term implantation in certain animal species. There is a clear need for tests which will predict calcification prior to such late animal or clinical experience. Several types of in vitro systems have been proposed to mimic the calcification process in humans. The validity of these systems remains to be demonstrated. In all studies, it is important to demonstrate that when calcification is observed, it is due to an intrinsic process rather than as a consequence of infection.

It is anticipated that a variety of approaches and expertise could be brought to bear on the solution of this problem. Among the disciplines and expertise which may be appropriate are calcium metabolism, immunology, hematology, pathology, surgery, veterinary medicine, and the physical, chemical and engineering sciences. Each research program supported by this mechanism should have a very focused approach to answer the proposed hypothesis rather than an all-encompassing approach with multiple projects. Domonstrated expertise in the methodologies proposed is advantageous. The roles of all personnel should be clearly identified. If collaborative or subcontracting arrangements are proposed, the effort and justification for all such personnel and other budget items should be specified; all subcontracting arrangements should include authorized signatures from the subcontracting facility which indicate their commitment to the proposed research should a grant be awarded. A clear time plan for staging experiments, plans for integrating experimental results at each stage, the types of controls which will be used for all parameters to be studied, the numbers of replicate experiments required for meaningful interpretation of results, and criteria for acceptance or rejection of the hypothesis should be specified.

III. MECHANISM OF SUPPORT

The support mechanism of this program will be the NIH research project grant. This type of announcement (the RFA) is used when the Institute--with the concurrence of its National Advisory Council--wishes to stimulate investigator interest in a particular research problem that is important to its program. The RFA solicitation represents a single competition with one specified deadline for receipt of application with all applications to be reviewed by the same initial review group. Although this announcement is included and provided for in the financial plans for FY 1982, support of grants pursuant to this Request for Applications is contingent upon ultimate receipt of appropriated funds for this purpose. The total annual funding level for the program is estimated at $650,000. A variety of approaches would be responsive to this solicitation; accordingly, it is anticipated that there will be a range of costs among the individual grants awarded. It is anticipated that 5 to 7 awards will be made if a sufficient number of high quality applications is received; this should be considered in the preparation of the scope of work and budget. The total project period should not exceed three years in duration; funds for those projects to be supported by this program will be awarded on September 30, 1982.

The RFA identifies the scope of the Institute's interest but does not require that the application conform to a specific protocol. Thus it is expected that each successful applicant will plan, direct, and carry out the research program. Applicants are requested to furnish their own estimates of the time required to achieve specific objectives of the proposed work and an outline of the phases or segments into which the proposed project can be logically divided.

As with any research grant, the recipient must obtain prior approval for any major change in the scope or objectives of the approved project. Applicants should be aware that this general requirement is particularly pertinent when, as in the case of RFA solicitations, the awarding Institute has committed funds in response to a specific program need. Ongoing evaluation may include periodic staff visits and the review of formal progress reports. In addition, it is anticipated that participants will exchange information and identify opportunities for collaboration. Applicants should request support to attend an annual two-day research meeting for this purpose; such a meeting would most likely be held in Bethesda, Maryland.

Unless specifically stated to the contrary herein, all policies and requirements which govern the grant program of the PHS apply, including the requirement for cost sharing.

IV. REVIEW PROCEDURES AND CRITERIA

Applications will be reviewed in a national competition with each other. Primary review will be conducted by an Initial Review Group composed primarily of non-Federal scientific consultants. Secondary review will be by the National Heart, Lung, and Blood Advisory Council. Applicants will be informed of the results of the competition as soon as possible after the September, 1982 meeting of the Council.

The major factors considered in evaluating each application will be:

1. The scientific merit of the application to elucidate the mechanisms of calcification of prosthetic materials in the cardiovascular system; that is, the proposed hypothesis, the research design and approaches, the methodology, and the analysis and interpretation of data.

2. The research experience and competence of the staff, including all collaborating investigators, to carry out the proposed investigations and the justification for the effort they will devote to the program.

3. The adequacy of existing and proposed facilities and resources, including proposed subcontractors.

4. The organizational and administrative structure of the proposed program, including timing of experiments and interrelationship and integration of subprojects.

5. Willingness to work cooperatively with other participants in the program.

6. Justification for the cost of the proposed research.

V. METHOD OF APPLYING

A. Letter of Intent

Prospective applicants are asked to submit a brief, one-page letter of intent which includes a very brief synopsis of the proposed areas of research and identification of any other participating institutions. This letter should be received no later than February 15, 1982 and addressed to:

Dr. Charles L. Turbyfill
Division of Extramural Affairs
National Heart, Lung, and Blood Institute
National Institutes of Health
Westwood Building, Room 553
5333 Westbard Avenue
Bethesda, MD 20205

The Institute requests such letters for the sole purpose of providing an indication of the number and scope of applications to be received. A letter of intent is not binding, and it will not enter into the review of any application subsequently submitted, nor is it a necessary requirement for application.

B. Format for Applications

Applications should be submitted on form PHS 398, the application form for a regular research grant. This form is available at the applicant's institutional office of sponsored research or from the Division of Research Grants, NIH. The conventional format of research grant applications should be utilized, ensuring that the points identified under "Review Procedures and Criteria" (see Section IV above) are fulfilled. In order to identify the application as a response to this RFA, check "yes" on Item 2 of the application face page with the tital MECHANISMS OF CALCIFICATION OF PROSTHETIC MATERIALS IN THE CARDIOVASCULAR SYSTEM and the RFA number NHLBI-DHVD-82G-H. Specific attention is directed towards the inclusion of a statement indicating the willingness of the applicant to exchange information with other participants in the program.

C. Application Procedure

The top of the face page of the applications and the outside of the mailing package should be labeled "Response to RFA NIH-NHLBI-DHVD-82G-H". The completed application and six (6) copies should be sent or delivered to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
5333 Westbard Avenue
Bethesda, MD 20205

To ensure their review, applications must be received by April 15, 1982. Applications not received by this deadline will be considered ineligible and, after discussion with the applicant, may be considered as a regular research grant application. If an application which is essentially identical has already been submitted to NIH for review, it must be withdrawn before the new application is accepted. Authors of applications that are considered to be nonresponsive to this announcement will be contacted to determine if they wish to have the application returned or reviewed as a regular research grant.

Applications will be accepted and reviewed as follows:

Application Receipt	Initial Review	Council Review	Start Date
April 15, 1982	June	September	September 30, 1982

VI. IDENTIFICATION OF CONTACT POINTS

Inquiries may be directed to:

Dr. Frances A. Pitlick
Devices and Technology Branch
Division of Heart and Vascular Diseases
National Heart, Lung, and Blood Institute
Federal Building, Room 312
Bethesda, MD 20205

Telephone: (301) 496-1586

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA RFA-NIH-NHLBI-82G-G

IMAGE ENHANCEMENT TECHNIQUES FOR VISUALIZATION OF CORONARY ARTERIES AND CORONARY BYPASS GRAFTS

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Application receipt date: April 15, 1982

The Division of Heart and Vascular Diseases of the National Heart, Lung, and Blood Institute invites grant applications for research involving image enhancement techniques to improve visualization of coronary arteries and coronary bypass grafts. Images of such arteries, their walls, and plaques encroaching upon lumens are often of poor quality and often the image is not clearly visualized because of background noise. The major thrust of this special grant program is to improve image quality by developing better image enhancement techniques. Among disciplines which may be appropriate in this research are mathematics, computer science, pattern recognition, and clinical expertise such as cardiology and radiology.

The Institute will use the grant-in-aid as the support mechanism, but it will differ from other research grants both in its goal orientation and in the expectation that grantees will exchange information and develop collaborations related to the research supported by this program. The present announcement is for a single competition with a specified deadline of April 15, 1982 for receipt of applications. It is open to all interested investigators, including those who are already the recipients of research grants from the NHLBI. Applications should be prepared and submitted in accordance with the aim and requirements described in the following sections. Section V of this announcement specified the method for applying.

I. BACKGROUND INFORMATION

A. The Diagnostic Instrumentation Program

The Devices and Technology Branch of the Division of Heart and Vascular Diseases of the National Heart, Lung, and Blood Institute has the responsibility for the design and administration of programs for research and development of diagnostic instruments applied to the heart and vascular system. The program fosters the development of new knowledge and the translation of results into methods which will have clinical application. A major component of this program is the research and development of instruments for detecting and quantifying atherosclerotic lesions in arteries. Imaging techniques have been especially emphasized. Several projects in this area are supported by grants as a result of investigator-initiated applications. In addition, targeted programs initiated by the Institute have led to support of a number of contracts in the same scientific area.

This program is described in the Catalog of Federal Domestic Assistance, No. 13.837, Heart and Vascular Diseases Research. Awards will be made under the authority of the Public Health Service Act, Section 301 (42 USC 241) and administered under PHS grant policies and Federal Regulations, most specifically 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse of Health Systems Agency review.

B. Historical Perspective

The areas of research currently supported by research grants include x-ray radiography techniques for studying cardiac structure and function, ultrasonic techniques for studying blood flow, and imaging methods for assessing atherosclerotic lesions. For several years, targeted programs for visualization of atherosclerotic lesions have been supported through research and development contracts. In 1977 several contracts were awarded for research and development of noninvasive methods for imaging arteries using ultrasound and x-ray techniques. The most recent contract awards were in later 1980 for research and development for noninvasive techniques for detection and quantification of atherosclerotic lesions in peripheral and coronary arteries. The eight contracts presently active include four which involve intravenous subtraction angiography, three involving ultrasound B-scan imaging, and one involving nuclear magnetic resonance imaging. In each of these contracts, emphasis is on detecting lesions in deep lying arteries, including coronary arteries.

II. RESEARCH GOALS AND SCOPE

This RFA is intended to encourage grant applications for research to improve image enhancement techniques applicable to images of coronary arteries and coronary bypass grafts.

Several instrumentation techniques which may be applied to imaging atherosclerotic lesions in arteries include ultrasound B-scanning, intravenous subtraction radiography, nuclear magnetic resonance, positron emission tomography, and nuclear medicine methods using radioisotopes. The image quality for each of these techniques is generally inferior to that obtained with intra-arterial angiography. Only when image enhancement techniques are applied can the images obtained approach the quality desired. These image enhancement techniques appear to be reasonably effective when applied to images of carotid or femoral arteries. Intravenous subtraction radiography, ultrasound B-scanning, and nuclear magnetic resonance are techniques which appear promising for coronary artery imaging. Instrument research now being supported by NHLBI indicates that detection of lesions in coronary arteries in humans will be possible using one or more of these less invasive techniques. The problems of close proximity to blood-filled ventricles, distance from arteries to skin surface, motion effects and small lumen diameter, among others, are factors which will contribute to the decreased quality of the resultant images. Additional research in image processing and enhancement techniques may extend present knowledge so as to allow a significant improvement in image quality. A desirable outcome would be that these improved techniques be generally applicable to images regardless of whether they are derived from x-ray, ultrasound, or other instrumentation.

Since coronary artery imaging using techniques other than intra-arterial angiography is in such an early stage of development, it is not possible to be precise regarding image quality. However, it appears that coronary artery images are and will continue to be "noisier" by a factor of five to ten as compared with carotid artery images. Included in the proposals should be the investigator's estimate of the expected level of improvement which may be achieved with the proposed image enhancement techniques. Also included should be quantitative methods for expressing image quality and plans for validation of the proposed technique. Validation should be directly related to demonstrating the improved diagnostic quality of coronary artery or coronary bypass graft images.

Investigators are encouraged to apply techniques which have been used in related high technology fields, e.g., space exploration, high altitude photography. Research and development in these areas may be partially or wholly applicable. Collaborative arrangements with profit-making institutions are possible through subcontrcts.

Applications are invited for any combination of theoretical studies, software development, phantom studies, studies in laboratory animals, or in the clinical setting. Proposals involving multidisciplinary research efforts are encouraged. Some of the disciplines that may be appropriate in this research include mathematics, pattern recognition, computer science, and clinical expertise, such as cardiology and radiology. New concepts and approaches are encouraged. In all instances, the perceived relationship and importance of the proposed work to the improved understanding of image processing and enhancement as related to coronary arteries and coronary bypass grafts should be made explicit.

The proposed research should be dedicated to improving quality of images which are obtainable using current technology. THERE IS NO INTENTION OF SUPPORTING MAJOR INSTRUMENT RESEARCH OR DEVELOPMENT. Applicants should include in their proposals evidence of previous feasibility studies, if applicable, as well as plans for evaluating the performance of the proposed image enhancement techniques.

Potential applicants should review their research proposals in the context of the enunciated program goals and review criteria to reassure themselves that their application is truly responsive. If it is not clearly responsive or the relevance and responsiveness of a research proposal to these goals and criteria are tenuous, the application should be considered for submission as a regular grant application. It should be recognized that the existence of a targeted program and the distribution of a request for grant applications does not preempt the topic from the regular research grant program.

Because this program is one in which the various elements have relevance to one another and may depend upon each other, free communication is expected among the participants. It is anticipated that participants will exchange information and identify opportunities for collaboration. In the preparation of the budget for the grant application, applicants should request travel funds for one, two-day research meeting each year, most likely to be held in Bethesda, Maryland.

III. MECHANISMS OF SUPPORT

The support mechanism for this program will be the NIH research project grant. This type of announcement (the RFA) is used when the Institute-with the concurrence of its national advisory council-wishes to stimulate investigator interest in a particular research problem that is important to its program. The RFA solicitation represents a single competition with one specified deadline for receipt of applications. All applications in response to an RFA are reviewed by the same initial review group usually for a designated amount of funds or number of awards.

The RFA identifies the scope of the Institute's interest but does not require that the proposal conform to a specific protocol. Thus it is expected that each successful applicant will plan, direct, and carry out the research program. As with any research grant, the recipient must obtain prior approval for any major change in the scope or objectives of the approved project. Applicants should be aware that this general requirement is particularly pertinent when, as in the case of RFA solicitations, the awarding Institute has committed funds in response to a specific program need. Ongoing evaluation may include periodic visits and the review of formal progress reports.

Applicants are requested to furnish their own estimates of the time required to achieve specific objectives of the proposed work and an outline of the phases or segments into which the proposed project can be logically divided. The total project period should not exceed three years in duration. A September 30, 1982 starting date for the project should be requested.

Although this announcement is included and provided for in the Institute's financial plans for Fiscal Year 1982, support of grants pursuant to this Request for Applications is contingent upon ultimate receipt of appropriated funds for this purpose. The total annual funding level for the program is estimated at $450,000. A variety of approaches would be responsive to this solicitation; accordingly, it is anticipated that there will be a range of costs among the individual grants awarded. It is anticipated that 4-6 awards will be made if a sufficient number of high quality applications is received; this should be considered in the preparation of the scope of work and budget.

Unless specifically stated to the contrary herein, all policies and requirements which govern the grant program of the PHS apply, including the requirements for cost sharing.

IV. REVIEW PROCEDURES AND CRITERIA

Applications will be reviewed in a national competition with one another. Primary review will be conducted by an Initial Review Group composed primarily of non-Federal scientific consultants. Secondary review will be by the National Heart, Lung, and Blood Advisory Council. Applicants will be informed of the results of the competition as soon as possible after the September 1982 meeting of the Council.

The major factors considered in evaluating each application will be:

1. The scientific merit of the application, that is, the theoretical basis for the proposed methodology, its implementation, and the analysis of its performance in improving image quality.

2. The level of improvement of image quality likely to be achieved and the proposed methods for quantifying image quality.

3. The proposed methods for validating how the described technique improves diagnostic quality of images of coronary arteries and coronary bypass grafts.

4. The research experience and competence of the staff to carry out the proposed investigations and the time they will devote to the program.

5. The adequacy of existing and proposed facilities and resources.

6. In applications containing more than one project, the integration of various projects into an effective total program.

7. The organizational and administrative structure of the proposed program, with a clear description of the responsibilities of each of the participating individuals.

8 Willingness to work cooperatively with other participants in the program.

9. Justification for the cost of the proposed research.

V. METHOD OF APPLYING

A. Letter of Intent

Prospective applicants are asked to submit a brief, one-page letter of intent which includes a very brief synopsis of the proposed areas of research and identification of any other participating institutions. This letter should be received no later than February 15, 1982, and sent to:

Dr. Charles L. Turbyfill
Review Branch, Division of Extramural Affairs
National Institutes of Health
Westwood Building, Room 553
5333 Westbard Avenue
Bethesda, Maryland 20205

The Institute requests such letters for the purpose of providing an indication of the number and scope of applications to be received. A letter of intent is not binding, and it will not enter into the review of any application subsequently submitted, nor is it a necessary requirement for application.

B. Format for Applications

Applications should be submitted on form PHS 398, the appliction form for a regular research grant. This form is available at the applicant's institutional office of sponsored research or from the Division of Research Grants, NIH. The conventional format of research grant applications should be utilized, ensuring that the points identified under "Review Procedures and Criteria" (see Section IV, above) are fulfilled. To identify the application as a response to this RFA, check "yes" on Item 2 of the application with the title IMAGE ENHANCEMENT TECHNIQUES FOR VISUALIZATION OF CORONARY ARTERIES AND CORONARY BYPASS GRAFTS and the RFA number NHLBI-DHVD-82-G-G. Specific attention is directed towards the inclusion of a statement indicating the willingness of the applicant to work cooperatively with other participants in the program.

C. Application Procedure

The completed application and thirty (30) copies thereof should be sent or delivered to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
5333 Westbard Building
Bethesda, Maryland 20205

To ensure their review, application must be received by April 15, 1982. Applications not received by this deadline will be considered ineligible and, after discussion with the applicant, may be considered as a regular research grant application. Concerning applications that are non-responsive to this announcement, applicants will be contacted to determine if they wish to have the proposal returned or reviewed as a regular research grant.

The outside of the mailing package and the top of the face page of the applications should be labeled "Response to RFA NIH-NHLBI-DHVD-82-G-G."

Applications will be accepted and reviewed as follows:

Application Receipt	Initial Review	Council Review	Start Date
April 15	June	September	September 30

VI. IDENTIFICATION OF CONTACT POINTS

Inquiried may be directed to:

Dr. Alan S. Berson
Devices and Technology Branch
Division of Heart and Vascular Diseases
National Heart, Lung, and Blood Institute
Federal Building, Room 312
Bethesda, Maryland 20205

Telephone: (301) 496-1586

ANNOUNCEMENT

FUNDING NOTICE

Congress and the President have agreed on a third Continuing Resolution affecting spending by agencies of the Federal Government during Fiscal Year (FY) 1982. The Resolution provides spending authority for the National Institutes of Health (NIH) until March 31, 1982, by which time a regular appropriation or a fourth Continuing Resolution must be enacted if NIH is to continue normal operations.

The Continuing Resolution requires NIH to achieve a 4 percent reduction in overall obligations under each of its appropriations from the lower of the proposed House or Senate levels, in contrast to the previous (second) Continuing Resolution which required a 12 percent reduction from the President's March, 1981 request for FY 1982 appropriations. Although detailed funding plans have yet to be developed, NIH expects to issue both new and continuation grant awards with an average 4 percent reduction between now and March 31, 1982. Partial restoration of reductions in previous FY 1982 awards that were based on the second Continuing Resolution will be made to bring them to comparable levels. These restorations will be made as soon as workload permits but in no case later than the end of February, 1982. The funds available for research and development contracts will also be reduced. Within this overall framework, there will be modest variations to accommodate the needs of individual award situations.

The current Continuing Resolution also will entail a reduction of approximately 4 percent in the funds for research training. The number of trainees NIH can support will be reduced by 3-4 percent. The institutional allowance associated with individual fellowships will be $3,000; the corresponding allowance for institutional fellowship awards (training grants) will be up to $2,500 per postdoctoral trainee and $1,500 per predoctoral trainee. Indirect cost reimbursement will remain at 8 percent of total allowable direct costs. There will be no change in the $2,000 allowance for individual fellowships at Federal institutions.

Awardees whose grants have a January 1 continuation start date, or whose competing award has been approved for a January 1 start date, may reasonably expect to receive reduced awards in line with the spending levels authorized by the Continuing Resolution. Awards will probably arrive late because of delayed preparation and slowdowns in holiday mail service. They will, however, be effective for the period beginning January 1, 1982.

NIH will publish additional notices as the details of FY 1982 funding plans are developed.

U.S. GOVERNMENT PRINTING OFFICE: 1982- 361-144:110

11/2

NIH GUIDE for GRANTS and CONTRACTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Vol. 11, No. 2, January 29, 1982

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HAVE YOU MOVED?

If your present address differs from that shown on the address label, please send your new address to: Grants and Contract Guide Distribution Center, National Institutes of Health, Room B3BN10, Building 31, Bethesda, Maryland 20205, and attach your address label to your letter. Prompt notice of your change of address will prevent your name from being removed from our mailing list.

The GUIDE is published at irregular intervals to announce scientific initiatives and to provide policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in grants and contracts activities administered by the National Institutes of Health.

Two types of supplements are published by the respective awarding units. Those printed on yellow paper concern contracts: solicitations of sources and announcement of availability of requests for proposals. Those printed on blue paper concern invitations for grant applications in well-defined scientific areas to accomplish specific program purposes.

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NIH GUIDE FOR GRANTS AND CONTRACTS
Vol. 11, No. 2, January 29, 1982

NOTICE

REVISED SUBMISSION PROCEDURE FOR GRANT APPLICATIONS

The Division of Research Grants has initiated a more efficient processing of the grant application form PHS 398. Your cooperation in following these revised submission instructions would be most helpful. The text of the new instructions follows:

> "Mail or deliver the complete and signed typewritten original of the application (including the CHECKLIST) and six signed, exact photocopies, in one package, together with six copies of any APPENDIX materials, to the Division of Research Grants, Room 240, Westwood Building, 5333 Westbard Avenue, Bethesda, MD 20205. The photocopies must be clear and single-sided. A preaddressed mailing label is provided in the application kit. Do not bind or staple the sets, but secure them with rubber bands or paper clips. Include the self-addressed three-part postcard, form PHS 3830, provided in the application kit." (Revisions underlined).

NOTICE

A CONFERENCE ON THE NIH CONTRACT AWARD AND ADMINISTRATION PROCESS

The NIH Division of Contracts and Grants and the University of Connecticut invite interested parties to attend a Conference sponsored by the University of Connecticut at their Storrs Campus on 29 and 30 April 1982. An actual NIH case study will be followed from initiation to completion.

AGENDA

DIFFERENCES BETWEEN CONTRACTS, GRANTS AND COOPERATIVE AGREEMENTS, MISCONCEPTIONS ABOUT CONTRACTS - Mr. Carl Fretts, Director, Division of Contracts and Grants, NIH

SEGMENT I - PROGRAM PLANNING, DEVELOPMENT, AND CONCEPT CLEARANCE - Dr. George Galasso, Chief, Development and Applications Branch, NIAID, and Mr. Lewis Pollack, Chief, Contract Management Branch, NIAID

SEGMENT II - REQUEST FOR CONTRACT TO RELEASE OF RFP - Mr. Lawrence Fitzgerald, Chief, Contracts Management Branch, NINCDS

SEGMENT III - DEVELOPMENT OF THE PROPOSAL FOR SUBMISSION - Mr. David Herman, Director, Office of Grants and Contracts, The University of Connecticut

SEGMENT IV - PROPOSAL RECEIPT AND EVALUATION - Mr. Curtis Tate, Deputy Director, Division of Contracts and Grants, NIH

RECEPTION AND DINNER — Faculty-Alumni Center

SEGMENT V - COMPETITIVE RANGE THROUGH CONTRACT AWARD - Mr. James Graalman, Chief, Research Contracts Branch, NCI

SEGMENT VI - POST AWARD CONTRACT ADMINISTRATION - Mr. Richard Wagner, Chief, Contracts Management Section, NICHHD

UPDATE ON CONTRACT TRENDS - Mr. Carl Fretts

To register, contact the following individual:

Mr. David E. Herman
Director
Office of Grants and Contracts
University of Connecticut
Storrs, Connecticut 06268

Telephone: (203) 486-4436

Registration fees are $135 for early registrants (before March 15) and $155 for late registrants.

Any questions may be directed to Mr. David Herman of the University of Connecticut or:

Mr. Carl A. Fretts
Director
Division of Contracts and Grants
National Institutes of Health
Building 31, Room 1B03
9000 Rockville Pike
Bethesda, Maryland 20205

Telephone: (301) 496-4422

Please note that this conference will review the entire contract award process. It is not one in the series of proposed "special topic" contract seminars being considered by NIH. These "special topic" seminars will be announced at a later date.

ANNOUNCEMENT

PREVENTIVE CARDIOLOGY ACADEMIC AWARD

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

APPLICATION RECEIPT DATE: April 1, Annually
LETTER OF INTENT: March 1 (Preceding Application)

The Division of Heart and Vascular Diseases, National Heart, Lung, and Blood Institute has initiated the Preventive Cardiology Academic Award to provide a stimulus for the development of a preventive cardiology curriculum in those schools of medicine and osteopathy that do not have one and to strengthen and improve the preventive cardiology curriculum in those schools that do. Each school of medicine or osteopathy in the United States and its possessions or territories is eligible to compete for one award for a project period that does not exceed five years. The number of awards made each year will depend upon the merit of the applications receive and availability of funds.

For the purposes of the Preventive Cardiology Academic Award, the term preventive cardiology is used to define the area of cardiovascular medicine having a special concern with the development of knowledge and the application of knowledge directed at the prevention of heart and vascular diseases. This includes the area of primary prevention of cardiovascular diseases in infants, children, and adults who are at risk of developing such diseases and the reduction of preventable complications or disability in persons who have already developed cardiovascular disease.

This award is intended to:

- encourage the development of a high quality preventive cardiology curriculum in schools of medicine and osteopathy that will significantly increase the opportunities for students and house staff to learn both the principles and practice of preventive cardiology;
- develop promising faculty whose interest and training are in preventive cardiology teaching, research, and practice;
- develop established faculty who have a major commitment to and possess educational skills for teaching preventive cardiology;
- facilitate interchange of educational ideas and methods applicable to teaching preventive cardiology among awardees and institutions;

This program is described in the Catalog of Federal Domestic Assistance No. 13.837, Heart and Vascular Diseases Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410 as amended; 42 USC 241) and Section 413 (42 USC 287b) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

- develop at the grantee institution the ability to strengthen continuously the improved preventive cardiology curriculum, with local funds, subsequent to the award.

CRITERIA FOR THE AWARD

Competitive review of proposals will include an evaluation of the evidence of commitment of both the sponsoring institution and the head of the cardiology division to the accomplishment of the objectives of the award as well as the qualifications, interest and commitment of the candidate to undertake responsibility for implementing a high quality preventive cardiology curriculum. Sponsorship of the candidate must be by the head of the division responsible for the teaching and practice of cardiology in the institution. Joint appointments with other departments or schools such as Preventive Medicine, Pediatrics or Epidemiology are encouraged when they would lead to a meaningful enhancement of the curriculum, extend concepts of prevention to other teaching areas or enhance the candidate's professional development in preventive cardiology teaching, research or practice. Multidisciplinary programs are encouraged.

The candidate must have sufficient clinical training and research experience in cardiology to be able to develop and implement a high quality curriculum within the institution. If the candidate's background requires further educational development, the plans to acquire this additional training should be described. Relevant training in epidemiology, clinical trials, behavioral science or other areas could be advantageous in the broader role of the candidate in stimulating preventive cardiology concepts among other peer health professionals in the institution.

PROVISIONS OF THE AWARD

The non-renewable Preventive Cardiology Academic Award will include funds for the awardee's salary, fringe benefits, funds for curriculum development, and actual indirect costs not to exceed 8% of total allowable direct costs.

The applicant may request salary support up to $30,000 per year. In addition to this amount, fringe benefits may be requested at the applicable institutional rate.

The applicant must devote a minimum of 50% time to this grant and the salary which is requested may not exceed the time or effort to be devoted to the Preventive Cardiology Academic Award. The total salary on which it is based must be consistent both with the established salary structure at the institution and with salaries actually provided by the institution from its own funds to other staff members of equivalent qualifications, rank, and reponsibilities in the department concerned. If full-time salaries are not currently paid to comparable staff members, the proposed salary must be appropriately related to the existing part-time salary structure. The awardee may devote up to 50% effort as principal or participating investigator on an NIH-supported grant(s) or contract(s) and may be remunerated from the grant(s) or contract(s) accordingly.

Developmental funds may include personnel support necessary to achieve the program objectives; travel funds to enable the awardee to visit other institutions or to attend special meetings, courses or conferences designed to increase his/her knowledge and competence in the teaching/learning process related to preventive cardiology; equipment necessary as teaching aids; supplies necessary to the program objectives; and stipends for a limited number of students to extend their preventive cardiology learning experience during their elective quarter in the academic year. Funds may not be used to support cardiology fellowships or research projects.

REVIEW OF APPLICATIONS

Applications for initial Preventive Cardiology Academic Awards will be appraised in terms of criteria outlined for the institution and the awardee in **Criteria for the Award.**

The review will include an initial assessment of the written proposal and an interview with the prospective awardee in Bethesda, Maryland by the Research Manpower Review Committee managed by the Division of Extramural Affairs of NHLBI. (Travel expenses for this interview must be paid by the applicant institution.) When necessary, a site visit may be made to the institution to determine the institutional environment, the commitment of the sponsoring division or department head and evidence of cooperation that may be needed to implement the candidate's proposed program. The initial review group will recommend applicants for consideration to the National Heart, Lung, and Blood Advisory Council.

METHOD OF APPLYING

Each prospective applicant should forward a letter of intent, countersigned by the head of the cardiology division or department, by March 1 preceding the receipt date to:

Dr. Carol Letendre
Contracts, Clinical Trials, and Training
Review Section
Review Branch, Division of Extramural Affairs
National Heart, Lung, and Blood Institute
Westwood Building, Room 548
Bethesda, Maryland 20205

These letters will not be considered commitments but will be used to estimate the number of proposals to be submitted.

Applications for Preventive Cardiology Academic Awards may be submitted for the April 1 receipt date each year to the National Institutes of Health for review by the National Heart, Lung, and Blood Advisory Council the following September. The requested beginning date for funding should be July 1 of the year following the receipt date.

Application forms (PHS 398) may be obtained from the administrative office of the applicant institution or from the Division of Research Grants, NIH.

DEADLINE FOR RECEIPT OF APPLICATIONS

Beginning in April 1980, the annual receipt date was established as follows:

APPLICATION RECEIPT	COUNCIL REVIEW	START DATE
April 1	September	July 1*

* Of the year following application receipt.

FOR ADDITIONAL INFORMATION

Prospective applicants are encouraged to review the Preventive Cardiology Academic Awards Guidelines dated December 1, 1981, which detail the eligibility requirements and application procedures. Requests for copies of these guidelines and questions related to Preventive Cardiology Academic Award should be directed to:

Dr. William T. Friedewald
Acting Chief, Preventive Cardiology Branch
Division of Heart and Vascular Diseases
National Heart, Lung, and Blood Institute
Federal Building, Room 212A
Bethesda, Maryland 20205

Telephone: (301) 496-2533

REQUEST FOR RESEARCH GRANT APPLICATIONS (RFA)

USE OF PERFLUOROCHEMICALS IN BASIC AND APPLIED RESEARCH

DIVISION OF BLOOD DISEASES AND RESOURCES

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

APPLICATION RECEIPT DATE: June 1, 1982
LETTER OF INTENT: March 1, 1982

The Division of Blood Diseases and Resources (DBDR) sponsors fundamental and clinical research grants and contracts related to the characterization, preservation, and use of blood and its components. The Division's research interests are directed toward improvement of blood fractionation, development of new fractionation products, improvement of the storage of blood and its products, proper use of blood components in therapy, and elimination of the hazards of blood transfusion (with special emphasis on the problem of posttransfusion hepatitis). The Division also sponsors research related to the synthesis, screening, and biological activity of artificial blood substitutes. The present RFA, however, is intended to foster fundamental and applied research using available perfluorochemical blood substitutes as research tools.

This RFA, which will use the customary grant-in-aid mechanism of the National Institutes of Health, will be governed by the policies for regular research grants. The responsibility for planning, directing, and executing the proposed research project will be solely that of the applicant.

The present RFA announcement is open to all interested investigators and will feature a single competition with a specified deadline for receipt of applications. It is anticipated that all applications in response to the RFA will be reviewed at the same time by a single review panel. Funded applications will be considered as regular research grants, with the exception that cooperation between investigators and the staff of the National, Heart, Lung, and Blood Institute (NHLBI) will be encouraged.

In contrast to the standard procedure for submission of regular applications for research grants, potential applicants are requested to send, by March 1, 1982, a letter of intent to submit an application. The original and 6 copies of the application are to be sent to the Division of Research Grants and 18 copies are to be sent to Dr. Charles L. Turbyfill. The deadline for receipt of applications is June 1, 1982. A brief covering letter should be

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This program is described in the Catalog of Federal Domestic Assistance No. 13.839, Blood Diseases and Resources. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

enclosed indicating that the application is being submitted in response to the RFA NHLBI-DBDR-82G-I: USE OF PERFLUOROCHEMICALS IN BASIC AND APPLIED RESEARCH. Applications should be prepared in accordance with the aims and requirements described in the following sections:

I. BACKGROUND INFORMATION
II. GOALS AND SCOPE
III. MECHANISM OF SUPPORT
IV. REVIEW PROCEDURES AND CRITERIA
V. METHOD OF APPLYING
VI. INQUIRIES

I. BACKGROUND INFORMATION

In 1966, Clark and Gollan demonstrated that mice survived when totally immersed in an oxygenated liquid perfluorochemical (1). Later, it was shown that rat hearts remained viable in vitro when alternately perfused with oxygenated perfluorochemical and with aqueous perfusion fluid (2). Sloviter and Kamimoto were able to sustain rat brain in vitro for several hours by perfusion with perfluorochemical dispersed in serum (3). These classic experiments established the potential usefulness of these compounds.

Perfluorochemicals consist of hydrocarbons or other organic compounds in which all hydrogen atoms have been replaced by fluorine atoms. Oxygen is so highly soluble in most liquid perfluorochemicals that as much as 65 percent oxygen by volume can be dissolved in the undiluted perfluorochemical. By contrast, whole blood can dissolve approximately 20 percent oxygen, and saline or plasma only 3 percent.

Pure perfluorochemicals, however, are immiscible with blood. Nevertheless, Geyer showed that rats given an aqueous solution of perfluorochemical, pluronic polyols, electrolytes, glucose, and antibiotics to replace the total blood volume could survive as long as eight hours without being given plasma proteins or blood cells (4). The pluronic polyols not only helped emulsify the perfluorochemical but also contributed to the oncotic pressure. Changing the composition of the blood substitutes, altering the flow characteristics, and introducing hydroxyethyl starch (HES) has also been studied by Geyer in completely exchanged (bloodless) rats. These rats not only survived the removal of all blood constituents but also were active and alert in the postexchange period; they performed such normal functions as eating, drinking, washing, and urinating. The animals continued to live and regenerate normal red cells and plasma proteins and to grow and develop normally (5). These findings provided the major impetus for the practical use of perfluorochemicals as oxygen-carrying red cell substitutes.

Recently, emulsions of perfluorochemical have been administered to humans, with encouraging results. Makowski et al. (6) administered, without untoward reactions, a commercially prepared perfluorochemical emulsion (trade name Fluosol-DA) to seven decerebrate humans. Similarly, Ohyanagi et al. (7) successfully infused Fluosol-DA in ten healthy adult male volunteers.

Fluosol-DA has been used with apparent success in approximately 200 surgical patients in Japan and over 20 Jehovah's Witnesses patients in the United States suffering from blood loss or anemia. A few case reports recently have appeared in the literature; however, information from well-controlled clinical trials is still lacking.

Fluosol-DA consists of a mixture of two perfluorochemical compounds, perfluorodecalin and perfluorotripropylamine. Perfluorotripropylamine stabilizes the emulsion; however, the half-life in the body is approximately 65 days, which is longer than is desirable for clinical use in humans. The DBDR is currently supporting studies to develop improved emulsions that are more rapidly eliminated from the body and to search for new perfluorochemical compounds devoid of other undesirable physiological properties.

References

1. Clark, L.C., Jr., and Gollan, F.: Survival of mammal breathing organic liquids equilibrated with oxygen at atmospheric pressure. Science 152:1755-1756, 1966.

2. Gollan, F., and Clark, L.C., Jr.: Organ perfusion with fluorocarbon fluid. Physiologist 9:191, 1966.

3. Sloviter, H.A., and Kamimoto, T.: Erythrocyte substitute for perfusion of brain. Nature (London) 216:458-460, 1967.

4. Geyer, R.P., Monroe, R.G., and Taylor, K.: Survival of rats totally perfused with a fluorocarbon-detergent preparation. In Organ Perfusion and Preservation (J.C. Norman, ed.), pp. 85-96, Appleton, New York, 1968.

5. Geyer, R.P.: Studies and uses of perfluorochemical emulsions as blood substitutes. In Proceedings of HS Symposium on Research on Perfluorochemicals in Medicine and Biology, April 28-29, 1977, Stockholm (Novakova, V., and Plantin, L.O., eds.), Karolinska Institute Research Center, Huddinge, Sweden, pp. 229-279, 1978.

6. Makowski, H., Tentschev, P., Frey, R., Necek, S.T., Bergmann, H., and Blauhut, B.: Tolerance of an oxygen-carrying colloidal plasma substitute in human beings. In Proceedings of the IVth International Symposium on Perfluorochemical Blood Substitutes 1978, Kyoto, Excepta Medica (publisher), Amsterdam, pp. 47-53, 1978.

7. Ohyanagi, H., K. Toshima, M. Sekita, M. Okamoto, T. Itoh, T. Mitsuno, R. Naito, T. Suyama and K. Yokoyama: Clinical studies of perfluorochemical whole blood substitutes: Safety of Fluosol-DA (20%) in normal human volunteers. Clinical Therapeutics 2, 306-312, 1979.

II. GOALS AND SCOPE

Substantial efforts have gone into the synthesis and screening of new perfluorochemical compounds for use as potential blood substitutes. It is not the intent of this RFA to foster similar studies, but, rather, to encourage urgently needed fundamental and applied research using the perfluorochemical-exchanged animal as a basic research tool. Although perfluorochemicals have been available for several years, relatively few fundamental studies involving bloodless animals have been performed. This situation is a result, in part, of the small number of investigators in the field. Some areas of interest are summarized in the following paragraphs and should serve as guidelines to the type of studies that may be appropriate. These examples represent only a sampling of the type of work that would be responsive to the goals of this RFA; investigators are also encouraged to consider other studies and approaches.

The use of animals made bloodless with perfluorochemical emulsions has yielded important new information. For example, rats exchanged with perfluorochemical emulsions were shown to survive in 10 percent or higher concentrations of carbon monoxide. This experiment demonstrated, for the first time, that carbon monoxide kills by anoxia rather than at the cellular level. This technique has enabled the study of the effects of acute and chronic carbon monoxide exposure without the complications of carboxyhemoglobin formation and anoxia. Additional studies in this area are needed and encouraged.

In bloodless rats, the number of erythrocytes recovered during total exchange perfusion with perfluorochemical exceeds the number of erythrocytes calculated to be present at the start of the experiment. These additional cells are predominantly reticulocytes. Similar recovery data have been obtained with leukocytes, platelets, and plasma proteins. Studies involving the effects of partial or total removal of blood cells or plasma proteins are of interest and would be responsive to the goals of the RFA. For example, the kinetics of cellular or plasma protein synthesis could be examined under precisely controlled conditions. Moreover, the sequence in which different blood components return to the circulation starting at essentially zero concentration could be followed.

The discovery that the temporary loss of gamma globulin and the reduction in the number of leukocytes in bloodless rats does not give rise to infections is of interest and requires further study. Furthermore, the findings that the loss of clotting factors after exchange did not result in abnormal bleeding in the rat is an extremely interesting phenomenon and one that deserves further investigation.

In cases of vascular occlusions such as embolism and atherosclerosis, perfluorochemical substitutes could improve oxygen transport because the finely dispersed perfluorochemical may enter affected areas more readily than does whole blood. Studies of its use in cerebrovascular occlusion would be of particular interest, especially in the light of results already obtained which demonstrate that perfluorochemicals reduce myocardial ischemic damage after experimental coronary occlusion.

In the hypertension area, abnormal sodium and potassium ion fluxes in cells such as erythrocytes have been proposed as indices of elevated blood pressure. The use of bloodless animals may be useful in elucidating this phenomenon.

Blood substitutes may also be used in the study of hematopoiesis, the transport of biologically active molecules, the functions of enzymes in circulation, and factors affecting the blood-brain barrier. The treatment of toxemias could benefit from temporary replacement of total blood volume. This technique has been used in cases of hepatic coma, where the patient's body temperature is lowered and oxygenated saline-albumin is employed as the replacement preparation. Such treatment is of short duration. With a satisfactory artificial blood substitute, long-term total-body perfusion would be possible at normal body temperature. Moreoever, it would not be necessary to replace the substitute with normal blood once the perfusion had been ended.

Organ perfusion and preservation are areas of immediate application for substitutes. Whether for transplantation or for studies on organ metabolism, the ability to maintain well-functioning organs in vitro is an important goal. Blood substitutes would free erythrocytes and plasma (serum) for other purposes and also offer more convenience than the natural materials. Adverse alteration of normal blood components by pumps, oxygenators, filters, and other equipment could be avoided if stable artificial mixtures were used rather than blood.

The examples cited above illustrate the potential of blood substitutes in medical research and the type of research projects that would fulfill the objectives of this program. Investigators are encouraged to consider other approaches. In the event applications related to the scientific programs of other Institutes are received, review and potential support by those Institutes or joint review and support with the NHLBI will be arranged as appropriate.

The major thrust of this initiative is to encourage work in areas where perfluorochemicals may have potential research use other than merely as a blood replacement solution. The Division is currently supporting several studies on the potential clinical use of perfluorochemicals as red cell substitutes. Those perfluorochemicals which have been shown in documented studies to be effective substitutes are to be utilized by applicants. A list of suitable perfluorochemicals and their respective manufacturers will be made available to interested applicants upon request.

III. MECHANISM OF SUPPORT

The support for this program will be the traditional grant-in-aid of the National Institutes of Health. Applicants, who will plan and execute their own research programs, are requested to furnish an outline of the segments into which the program can be logically divided, and their own estimates of the time required to achieve specific objectives of the proposed work.

The total project period of this proposal must not exceed three years. A starting date of September 30, 1982, should be requested.

Although this RFA is included in the Institute's financial plans for fiscal year 1982, support of grants pursuant to this RFA is contingent upon ultimate receipt of appropriated funds for this purpose. The award of grants will be influenced by the amount of funds available to the Division, by the overall merit of proposals, and by their relevance to the program goals. A variety of approaches would be responsive to this announcement; accordingly, a range of costs are expected among individual grants awarded. It is anticipated that approximately 4 to 5 grants will be awarded.

IV. REVIEW PROCEDURES AND CRITERIA

A. Review Method

The applications will be evaluated on a competitive basis. The primary review, which will be arranged by the Division of Extramural Affairs, NHLBI, will be by a group of predominantly non-Federal consultants with appropriate scientific expertise. Secondary review will be by the National Heart, Lung, and Blood Advisory Council no later than September 1982.

B. Review Criteria

Applications must be responsive to this RFA in that they must be relevant to the goals of this RFA. In addition, the following factors will be considered:

- scientific merit of the research design, approaches, and methodology;

- methods of analysis;
- adequacy of existing and proposed facilities and resources;
- research experience and competence of the staff to conduct the proposed investigations;
- adequacy of time (effort) to be devoted to the project by the investigators and the technical staff;
- availability of patients, where relevant;
- evidence of institutional commitment to the program;
- cost reasonableness of the program; and
- willingness to cooperate and coordinate with other investigators.

V. METHODS OF APPLYING

A. Letter of Intent

Prospective applicants are asked to submit a brief one-page letter of intent, which should include a very short synopsis of proposed areas of research and identification of any other participating institutions. This letter should be received no later than March 1, 1982, at the following address:

Dr. Charles L. Turbyfill
Westwood Building, Room 553
National Institutes of Health
Bethesda, Maryland 20205

The Institute requests such letters only to provide an indication of the number and scope of applications to be received. A letter of intent is not binding; it will not enter into the review of any proposal subsequently submitted nor is it a requirement for application.

B. Format for Application

Applications must be submitted on Form PHS-398, the application form for the traditional research grant. Application kits are available at most institutional business offices or from the Division of Research Grants, NIH. The format and detail suitable for regular research grant applications should be used, with care taken to satisfy the points listed under Review Criteria. Grantees will be expected to meet periodically and share results with other participants in the program and with the National Heart, Lung, and Blood Institute.

C. Application Procedure

The original and six copies of the completed application should be sent or delivered to:

Division of Research Grants
Westwood Building, Room 248
National Institutes of Health
Bethesda, Maryland 20205

Eighteen copies of the completed application should be sent or delivered to Dr. Charles L. Turbyfill whose address appears in section V.A. of this RFA.

Applications must be received by June 1, 1982.

Label the outside of the mailing package and the top of the face page "Response to RFA, NIH-NHLBI-DBDR-82G-I."

A very brief covering letter must accompany the application indicating that it is submitted in response to this RFA, NIH-NHLBI-DBDR-82G-I: "USE OF PERFLUOROCHEMICALS IN BASIC AND APPLIED RESEARCH." A carbon copy of this covering letter should be sent to Dr. George J. Nemo at the address below.

Schedule Summary:

Letter of Intent	March 1, 1982
Deadline for Receipt of Applications	June 1, 1982
Award	September 30, 1982

VI. INQUIRIES

Inquiries may be directed to:

Dr. George J. Nemo
Federal Building, Room 5C04
National Institutes of Health
Bethesda, Maryland 20205

Telephone Number: (301) 496-1537

ANNOUNCEMENT

AVAILABILITY OF REQUEST FOR APPLICATIONS (RFA)

CANCER CONTROL RESEARCH UNITS FOR DEFINED POPULATIONS

NATIONAL CANCER INSTITUTE

APPLICATION RECEIPT DATE: July 15, 1982
LETTER OF INTENT; MARCH 31, 1982

The National Cancer Institute (NCI) announces the availability of a Request for Applications (RFA) inviting proposals for the establishment of Cancer Control Research Units For Defined Populations.

The RFA will be available on or before January 31, 1982. Letters of intent will be required and will be due not later than March 31, 1982.

The Division of Resources, Centers and Community Activities (DRCCA) of NCI has developed a "Statement on Cancer Control (January 1981) which sets forth the general scope and definition of cancer control research. Briefly,

> "The goal of a cancer control program is to reduce cancer incidence, morbidity, and/or mortality by: 1) identifying approaches that might accomplish this and performing research in defined populations to determine which are effective, 2) selective promotion and evaluation of these approaches, and 3) selective education and information dissemination for health professionals and/or the public. The scope of cancer control includes prevention, screening, diagnosis, pretreatment evaluation, treatment, rehabilitation, and continuing care activities."

The purpose of this RFA is to encourage the development of Cancer Control Research Units (CCRU) for Defined Populations. Grants under this RFA will support a limited number of geographically dispersed CCRUs which will be designed to plan and implement cancer control research for defined populations and to serve as a resource for the cancer control research program of the National Cancer Program. At present, no comparable research units exist which are devoted to cancer control research of this kind.

The CCRU is designed to provide support for: a core group of researchers who have access to defined population(s) for cancer control research; several research projects which are judged to be meritorious in the peer review process; developmental funds for pilot projects which hold promise of being recommended for funding through the peer review process; and other resources, such as data support, which can be justified as necessary to achieve the goals of the CCRU.

This program is described in the Catalog of Federal Domestic Assistance No. 13.399, Cancer Control. Awards will be made under the authority of the Public Health Service Act, Title IV, Section 403 (Public Law 78-410, as amended; 42 USC 284) and administered under PHS grant policies and Federal regulations 42 CFR Part 52 and 45 CFR Part 74. This progam is not subject to A-95 Clearinghouse or Health Systems Agency review.

A defined population is a population which is characterized in terms of: numbers and methods of identifying individuals in the population; demographic characteristics such as age, sex, color, ethnic group; social and economic factors such as occupation, education, socioeconomic status; vital statistics such as incidence, morbidity, and/or mortality; personal or life style factors such as diet or smoking; genetic and/or biological characteristics or other factors associated with disease. For this RFA, there must be methods for identifying the population denominators and the occurrence of cancer within the population. The population may be defined either geographically, or by exposure, or by characteristics proven to have a statistical association with cancer.

The DRCCA, NCI, intends to support these CCRUs as grants for project periods of up to five years. It is anticipated that a maximum of approximately five awards will be made as a result of this request. Adjustments in the level of funding may be made annually. Renewal of the initial award beyond five years will be contingent upon satisfactory review of a competing renewal application by a peer review committee and availability of funds.

An RFA will be available on or before January 31, 1982 which outlines in greater detail the proposed study, the eligibility for application, the letter of intent procedure, and the review procedures and criteria. A letter of intent and discussions with Program staff will be required before a grant application can be submitted. An institution wishing to participate in this effort must submit an application in accordance with the guidelines specified in the RFA.

Additional information and copies of the RFA may be obtained from:

Carlos E. Caban, Ph.D.
Program Director
Cancer Centers Branch
Division of Resources, Centers and
Community Activities
National Cancer Institute
Blair Building, Room 716B
8300 Colesville Road
Silver Spring, Maryland 20910

Telephone: (301) 427-8663

STATEMENT ON CANCER CONTROL

DIVISION OF RESOURCES, CENTERS AND COMMUNITY ACTIVITIES

January 1981

The goal of a cancer control program is to reduce cancer incidence, morbidity, and/or mortality by: 1) identifying approaches that might accomplish this and performing research in defined populations to determine which are effective, 2) selective promotion and evaluation of these approaches, and 3) selective education and information dissemination for health professionals and/or the public. The scope of cancer control includes prevention, screening, diagnosis, pretreatment evaluation, treatment, rehabilitation and continuing care activities.

The national cancer effort includes both research into and application of control methods. These are complimentary and not antagonistic activities and are part of an ordered sequence, as indicated in the following statement from the report of the President's Biomedical Research Panel:*

> "The continuum from the discovery of new knowledge to the application of such knowledge in health care includes a number of steps:
>
> 1. discovery, through research, of new knowledge and the relating of new knowledge to the existing base;
> 2. translation of new knowledge, through applied research, into new technology and strategy for movement of discovery into health care;
> 3. validation of new technology through clinical trials; (through clinical trials in defined populations, and in other ways);**
> 4. determination of the safety and efficacy of new technology for widespread dissemination through demonstration projects;
> 5. education of the professional community in proper use of the new technology and of the lay community on the nature of these developments; and
> 6. skillful and balanced application of the new developments to the populations."

Cancer control includes 2 through 5 although different relative emphasis may be placed on each of those points depending on the specific cancer and whether prevention or treatment efforts are involved. Control and research must be mutually reinforcing and only the coordinated planning and implementation of research and control strategies will assure maximum yield from the dollars invested, maximum quality of the activities supported, and maximum probability that the research effort will continue to provide advances suitable for future application in the control of cancer.

Cancer control should support three types of activities in defined populations:

1. research to determine whether and to what extent, actions proposed for a particular cancer are effective;
2. research to determine the optimal strategies for promoting actions proven efficacious for particular cancers; and
3. selective implementation of those promotional strategies proven efficacious for particular cancers.

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* Report of the President's Biomedical Research Panel. Submitted to the President and the Congress of the United States. April 30, 1976. U.S. Department of HEW, Public Health Service, DHEW Pub. No. (05)76-500.

** Words in parentheses added by Subcommittee on Cancer Control, Board of Scientific Counselors, DRCCA, NCI, January 20, 1981.

Cancer control efforts should give priority to cancers meeting one or both of the following criteria: 1) cancers causing the greatest mortality/morbidity in the United States; 2) cancers for which apparently effective actions are available. Highest priority should be given to cancers meeting both criteria.

Current "optimal" techniques for preventing or treating cancer must be considered as imperfect and as in a constant state of evolution. Despite this fact, great benefit could be derived if the entire population had access to current "optimal" techniques. One aspect of cancer control is, therefore, to determine, by expert consensus, the currently acceptable standard of management for all aspects of the health care continuum for particular cancers. Discrepancies between this baseline standard of management (BSM) and the actual management practiced in particular communities can be ascertained and appropriate steps taken to achieve the baseline. Attempts to do this must, however, be predicated on the understanding that the baseline is dynamic and that today's standard is tomorrow's outmoded technology.

In the portion of the continuum concerned with diagnosis and treatment, the baselines standard of management may be represented by well designed clinical research protocols. One aspect of cancer control will, therefore, be the establishment of mechanisms that make it possible for community physicians to place patients on protocol studies, thus facilitating the implementation of current baseline standards of management.

In the portion of the continuum concerned with cancer prevention, it will be necessary to develop an understanding of human health behavior and to support research to identify strategies that effectively promote good health behaviors or effectively modify inappropriate health behaviors.

Another aspect of cancer control will be continuing assessment of the quality of important services and technologies, such as laboratory and x-ray. Standards for the quality of such services should be established as a part of the baseline standard of management and efforts made to ensure compliance with such standards through education of health professionals and the general public. These baseline standards are also in a state of evolution and will require revisions consistent with the advance of knowledge.

Social action for cancer control is another major channel that should be pursued. It includes such steps as reduction of occupational exposures to carcinogenic agents, a linking of institutional and community health agencies in the interest of cancer control, social and physical rehabilitation and supportive care of cancer patients, and the establishment of hospice programs for patients with terminal cancer.

The development of an effective national program for cancer control requires qualified personnel, particularly with training and experience in the disciplines of epidemiology, biostatistics, and disease control administration, and the placement of these individuals in responsible positions.

ANNOUNCEMENT

RESEARCH RELATED TO GENETIC SUSCEPTIBILITY TO HUMAN BREAST CANCER

NATIONAL CANCER INSTITUTE

The Breast Cancer Program of the National Cancer Institute encompasses the totality of problems related to the etiology, epidemiology, diagnosis, treatment, and prevention of breast cancer. This program has a special interest in stimulating investigator-initiated research grant applications (R01's) for investigations of genetic susceptibility to human breast cancer.

I. BACKGROUND INFORMATION

The clustering of breast cancer in families is a well-known phenomenon, and recent studies have indicated that in some families the disease appears to be segregating as a Mendelian trait, suggesting that one or more human genes are responsible for the susceptibility. Particular program interest in this area addresses such questions as: (1) what proportion of human breast cancers, female and male, may be accounted for or strongly influenced by susceptibility gene(s); (2) how many forms of genetic susceptibility exist and how common is each of these forms; (3) can the use of new genetic markers, including DNA polymorphisms, help to resolve these issues; (4) which, if any, environmental or cultural risk factors interact with genetic susceptibility; (5) how is genetic susceptibility expressed at physiological or biochemical metabolic levels; (6) how is genetic susceptibility expressed at the chromosomal or DNA level; (7) can new approaches in cloning, transfection, and/or somatic cell hybrids help to elucidate the molecular biology of genetic susceptibility; (8) does the natural history of genetically influenced breast cancer resemble that of non-familial breast cancer; (9) is increased familial risk reflected in breast cancer mortality risk; and (10) related questions about genetic aspects of human breast cancer.

II. MECHANISM OF SUPPORT

The mechanism of support will be the traditional research grant. Policies that govern research grant programs of the National Institutes of Health will prevail. The award of grants pursuant to this request for grant applications is contingent upon receipt of proposals of high scientific merit and the availability of appropriated funds.

This program is described in the Catalog of Federal Domestic Assistance No. 13.396, Cancer Biology. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

III. METHODS AND CRITERIA OF REVIEW

A. Assignment of Applications. Applications will be received by the Division of Research Grants (DRG), National Institutes of Health. DRG will refer the proposals to the appropriate Study Section for Scientific review, and will assign them to the National Cancer Institute for possible funding and management. These decisions will be governed by normal programmatic considerations as specified in the DRG Referral Guidelines.

B. Review Procedures. Applications in response to this announcement will be reviewed in accordance with the usual NIH peer review procedures (Study Section). The review criteria customarily employed by the NIH for research grant applications will prevail. Factors considered in the scientific merit evaluation of each application will include an assessment of the importance of the proposed research problem, the novelty and originality of approach, the training, experience and research competence of the investigator(s), the adequacy of experimental design, the suitability of the facilities, and the appropriateness of the requested budget relative to the work proposed. Following Study Section review, the application will be evaluated for program relevance by staff members of the Breast Cancer Program, NCI. Funding decisions will be based upon relative scientific merit, program relevance, and the Institute's ability to fund.

C. Deadlines. Applications will be accepted in accordance with the usual dates for new applications on an indefinite basis:

March 1 July 1 November 1

IV. METHOD OF APPLYING

Applications should be submitted on form PHS-398, which is available in the business or grants office at most academic or research institutions, or from the Division of Research Grants, NIH.

The phrase "PREPARED IN RESPONSE TO NCI ANNOUNCEMENT ON GENETIC SUSCEPTIBILITY TO HUMAN BREAST CANCER" should be typed across the top of the first page of the application. The original and six copies should be sent or delivered to:

Application Receipt Office
Division of Research Grants
National Institutes of Health
Room 240 - Westwood Building
5333 Westbard Avenue
Bethesda, Maryland 20205

In order to alert the Breat Cancer Program to the submission of proposals as requested above, copies of the face page and summary page of such applications should be forwarded under separate cover to:

Dr. Elizabeth P. Anderson
Chief, Epidemiology Projects Section
Breast Cancer Program Coordinating Branch
National Cancer Institute
Landow Building - Room 8C-17A
Bethesda, Maryland 20205

ANNOUNCEMENT

AREAS OF RESEARCH CONSIDERED PERIPHERAL TO THE NIEHS

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

This announcement will provide information to current grantees and prospective applicants for NIEHS funding regarding research areas no longer considered relevant to the programs of the Institute. While support has been provided in the past for a limited number of programs in the areas of research specified, new programs and competing renewals will not be considered for funding by the NIEHS. Ongoing projects will continue to receive support for the approved project period subject to budget negotiation and providing funds are available.

The NIEHS does not have responsibility for the following: (1) biological control of insects through the use of infectious agents or insect biochemistry; (2) studies on specific venoms or toxins which do not provide information and new knowledge of a universal nature regarding basic toxicological mechanisms and concepts; (3) research on natural or disturbed ecosystems; (4) studies dealing solely with environmental degradation or biotransformation of environmental pollutants, or the fate of contaminants and pollutants, including the origin, dispersion and disposition of noxious agents in the environment; (5) waterborne diseases of marine and freshwater fauna; and (6) projects representing purely chemical, physical or biological investigations not directly related to human environmental health problems.

Information regarding the programs and interests of the NIEHS may be obtained by contacting the Office of the Associate Director, Extramural Programs, NIEHS, P.O. Box 12233, Research Triangle Park, North Carolina 27709, Telephone (919) 541-7723, or Program Directors for specific programs at the address above:

Dr. Robert G. Owens - Special Programs
Telephone (919) 541-7825

Dr. Edward Gardner, Jr. - Regular Research Grants
Telephone (919) 541-7724

Dr. Christopher Schonwalder - Research Manpower Development
Telephone (919) 541-7634

FUNDING NOTICE

CLARIFICATION

The "funding notice" printed in the January 1 issue of the Guide (Vol. 11, No. 1, p. 42) described NIH funding plans under the third Continuing Resolution, through March 31, 1982. The funding strategy outlined in that notice will apply to awards with February 1 and March 1 start dates as well as the January 1 awards specifically mentioned.

The third sentence of the second paragraph referred to spending levels under the previous Continuing Resolution when in fact those levels were based on the President's revised 1982 budget figures submitted to Congress in September, 1981. The sentence should have read as follows:

> "Partial restoration of reductions in previous FY 1982 awards - based on Administration funding policy during the period covered by the second Continuing Resolution - will be made to bring them to comparable levels."

☆ U.S. GOVERNMENT PRINTING OFFICE: 1982-361-144:111

11/3

NIH GUIDE for GRANTS and CONTRACTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Vol. 11, No. 3, February 26, 1982

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The GUIDE is published at irregular intervals to announce scientific initiatives and to provide policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in grants and contracts activities administered by the National Institutes of Health.

Two types of supplements are published by the respective awarding units. Those printed on yellow paper concern contracts: solicitations of sources and announcement of availability of requests for proposals. Those printed on blue paper concern invitations for grant applications in well-defined scientific areas to accomplish specific program purposes.

HE 20.3008/2:

ANNOUNCEMENT

AVAILABILITY OF OPPORTUNITIES FOR AMERICAN SCIENTISTS TO PERFORM COLLABORATIVE RESEARCH OUTSIDE THE UNITED STATES

FOGARTY INTERNATIONAL CENTER

The John E. Fogarty International Center for Advanced Study in the Health Sciences (FIC) of the National Institutes of Health announces the availability of postdoctoral fellowships to U.S. health scientists who wish to conduct collaborative research abroad. The purpose of these fellowships is to enhance the exchange of research experience and information in the various biomedical and behavioral sciences. The types of activity that are supported by these programs include collaboration in basic or clinical research, and the familiarization with or utilization of special techniques and equipment not otherwise available to the applicant. Applications having any of the following as the major feature cannot be accepted: brief observational visits, attendance at scientific meetings, attendance in formal training courses, or independent research projects within the host country.

PROGRAMS

Five programs are available to U.S. citizens or permanent residents:

SENIOR INTERNATIONAL FELLOWSHIP (SIF)
(Supported and administered by the FIC)

SWEDISH MEDICAL RESEARCH COUNCIL FELLOWSHIPS (SMRC)
(Supported by the Government of Sweden)

SWISS NATIONAL SCIENCE FOUNDATION POSTDOCTORAL FELLOWSHIPS (SNSF)
(Supported by the Government of Switzerland)

FRENCH NATIONAL INSTITUTE OF HEALTH AND MEDICAL RESEARCH (INSERM) POSTDOCTORAL FELLOWSHIPS
(Supported by the Government of France)

NIH-FRENCH NATIONAL CENTER FOR SCIENTIFIC RESEARCH PROGRAM FOR SCIENTIFIC COLLABORATION (CNRS)
(Under an agreement between the NIH and the CNRS, the two organizations share in the support of U.S. and French scientists to work at laboratories in France and the U.S., respectively.)

ELIGIBILITY REQUIREMENTS

Applicants must meet the following requirements:

U.S. citizen or permanent U.S. resident;

Doctoral degree in clinical, behavioral or biomedical science;

Ten years or less or postdoctoral experience (SIF applicants should have five years or more postdoctoral experience not so specified for the CNRS);

Professional experience in the health sciences for at least two of the last four years (not so specified for the CNRS);

Affiliated with a U.S. public or private nonprofit research, clinical or educational institution (only required for SIF).

APPLICATION AND SELECTION

Applications for these programs are reviewed once annually. The receipt date for applications to the FIC Senior International Fellowship Program is June 1, 1982. The receipt date for all other applications is October 1, 1982. All applications are reviewed for scientific merit by the National Institutes of Health. The organization which provides financial support of the program selects candidates for participation. While the maximum period of support for all programs is one year, the minimum period of support varies with each program.

Information and applications are available from:

International Research and Awards Branch
Fogarty International Center
National Institutes of Health
Bethesda, Maryland 20205

Prospective applicants for the Senior International Fellowship Program, the FIC sponsored program, may obtain information brochures from the above address. Only the office of the dean or equivalent institutional official may request SIF fellowship applications which will be available from January 15 to May 15, 1982.

All correspondence should refer to specific programs and must be clearly marked using one of the following:

Senior Fellowships
Swedish Fellowships
Swiss Fellowships
INSERM
CNRS

For an expedient reply, please send a self-addressed label with your request.

NOTICE

NEW WORLD PRIMATE AVAILABILITY

As part of a major project in primate conservation and breeding, the Pan American Health Organization is providing services to South American countries in planning and operating wild primate management and primate breeding programs. These services are in part supported by the National Institutes of Health, in recognition of the need for international cooperation in conserving primates in their natural habitats as well as in research utilization. Programs have been initiated by Peru to protect endangered species such as Lagothrix flauvicauda (yellow-tailed woolly monkey), Cacajao rubicundus (red-faced uakari) and Callimico goeldii (Goeldi's marmoset). The Government of Peru has also established a program at Iquitos to breed monkeys and from which primate surveys and population monitoring are conducted. Another program is being developed in Columbia to bread Aotus trivirgatus (owl monkey), and extend previous nonhuman primate census work. As a consequence of their efforts, several species of primates are available to NIH grantees and contractors. These include:

Saimiri Sciureus
(gothic and roman arch squirrel monkeys) - colony produced and wild caught

Cebuella pygmaea
(pygmy marmoset) - colony produced and wild caught

Cebis appella
(brown capuchin) - wild caught

Saguinus fuscicollis
(saddle-back tamarin) - wild caught

Saguinus labiatus
(white lipped tamarin) - currently wild caught; colony produced animals will become available

Saguinus mystax
(moustached tamarin) - currently wild caught; colony produced animals will become available

Services can also be made available to scientists for conducting field studies relating to nonhuman primates with the assistance of program staff at Iquitos.

In order to assist Peruvian authorities in developing programs appropriate to meet future needs, users of New World primates are requested to inform the Interagency Primate Steering Committee (IPSC) of their projected requirements. Requests for animals and information concerning costs, and services that are available should be directed to:

Dr. Orland A. Soave
Executive Director, IPSC
National Institutes of Health
Building 31, Room 4B-30
Bethesda, Maryland 20205

Telephone: 301-496-5424

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

NIH-NIAID 82-5

SEXUALLY TRNSMITTED DISEASES RESEARCH UNITS

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Application Receipt Date: October 15, 1982

I. BACKGROUND INFORMATION

The National Institute of Allergy and Infectious Diseases (NIAID) invites applications for program project grants to be initiated during FY 1983 for participation in an ongoing program of research in Sexually Transmitted Diseases (STD). The policy of the NIAID states that program project proposals for STD research units will be received only at designated times. Support for proposals for creation of new STD research units, or for continuation of existing units, will be on a competitive basis. This RFA will be issued only once during fiscal year 1982.

One of the major health problems in the U.S. today is that of sexually transmitted (venereal) diseases. The explosive rise in gonococcal infections in the last decade, for example, has been considered a major infectious disease epidemic; it has been estimated conservatively that over 2,000,000 cases of gonorrhea occur each year, with the majority being unreported to public health agencies. Many other diseases are now also known to be transmitted by sexual contact and illness caused by them is being recognized with increasing frequency. Such diseases as genital herpes, hepatitis B, and group B streptococcal infections are examples of these. Nongonococcal urethritis (NGU) caused primarily by Chlamydia trachomatis and genital herpes are the most common of these infections, being second only to gonorrhea in numbers of cases.

The estimated cost of treating pelvic inflammatory disease (PID) may approach $1.25 billion per year, to say nothing of the thousands of women of childbearing age who are rendered sterile as a result of PID. Genital herpes infections in pregnant women at term pose a most serious hazard to the neonate. Group B streptococcal infection transmitted by the pregnant woman to her offspring at birth poses a similar hazard.

The burden of identifying and treating these diseases is a serious public health and economic problem. The hidden costs of sexually transmitted diseases in family disruption, absence from education or gainful employment, ill health and individual misery can only be imagined. Research offers one positive means of eventually controlling this public health problem.

The NIAID has been in the forefront in support of research in STD. The program has grown rapidly since its inception in 1971, indicative of a widespread recognition of research opportunities for increased understanding and control of these diseases. The NIAID program currently supports research in this area by program projects, individual research projects, contracts, training grants, and individual postdoctoral fellowships.

II. RESEARCH GOALS AND SCOPE

The goal of the program is to encourage investigators to undertake research tht will provide the clinical, epidemiological and microbiological information needed to control sexually transmitted diseases. The NIAID wishes to broaden the scope of its program in research so that the knowledge gained may be applied to improvement in the means of prevention, diagnosis, and therapy of these infections.

A. Requirements of the Research Program Project

As one means of achieving the stated goals, the NIAID proposes to maintain support of a number of STD research units, or centers of excellence, to serve as foci for research and training in STD. These units are funded as program project grants. The research to be considered for emphasis in this program can be on any or all of the STDs that are currently recognized as significant public health problems, as listed under "Research Scope."

A strong clinical component should be a major part of the program project application. There are several distinguishing characteristics that must be considered in developing these research units of excellence in STD:

1. They will be based at a teaching hospital or a university or medical school, or at a medical school affiliated hospital.

2. The program project will be multidisciplinary, combining the efforts of investigators in both clinical and basic science disciplines to focus on different facets of the overall problem of STD infections.

3. Integration and coordination of different departments within an institution usually will be necessary for adequate program development. Different collaborating institutions can also be involved. Close coordination and cooperation with a public venereal disease clinic (e.g., a city or county clinic) is of prime importance for successful functioning of the research unit.

4. The program project will consist of a number of individual subprojects, each with a clearly identified research task, and each with a principal investigator, staff, and budget.

   The program director will be responsible for the overall direction and administration of the total project. It is expected that the principal investigators of each of the subprojects will act as members of a strong and coordinated research team, the whole directed toward resolving some of the many problems in sexually transmitted diseases. The team concept is considered especially important in developing these program projects.

5. It is suggested that efforts be made to advance learning experiences in STD and to make medical students and doctoral candidates more aware of the needs and opportunities in STD research, at both the clinical and fundamental levels. A formal program of training that involves student stipends, however, will not be considered as part of this program. Formal training programs for both pre- and postdoctoral trainees are supported by a different funding mechanism.

Only institutions with demonstrated expertise in both clinical and basic sciences, and with strong, ongoing research programs and resources that can focus on a multidisciplinary and multifaceted attack on STD infections, will be considered for program project support under the provisions of this program.

B. Research Scope

The research efforts in this program will focus on the following diseases:

> Gonorrhea; syphilis; nongonococcal urethritis caused by chlamydial agents alone or in combination (e.g., Ureaplasma); Trichomonas infections; viral infections - genital herpes, genital warts and hepatitis B; nonspecific vaginitis; group B streptococcal infections; parasitic infestations; enteric or other diseases that may be recognized as transmitted by the sexual route.

The specific areas of research interest for the above STD problems will be:

1. Biology of the causal organisms - growth, nutrition, physiology and metabolism, antigenic structure, chemical composition.
2. Virulence factors of the microorganisms involved.
3. Antibody development and the role of humoral and cell mediated immune responses in the host.
4. Immunopathology of these diseases.
5. Pathogenesis and mechanisms of recovery and resistance; recurrent infections or reinfections.
6. Animal model systems for study of any facet of these diseases.
7. Immunodiagnosis - antigen detection, identification, specificity.
8. Therapy - immunotherapy - development of candidate vaccines or antisera. Development of more useful antimicrobial therapeutic modalities. Study of development of antibiotic resistance.
9. Epidemiology - of any of the STDs; this can include mathematical or computer modeling for useful control strategies.

Clinical and fundamental studies involving any or all of the above categories will be considered relevant to this program.

III. MECHANISM OF SUPPORT

Eligibility: Domestic universities, colleges, hospitals, laboratories, and other public or private institutions, including State and local governmental units, are eligible.

Length of Support: The project can be supported for a maximum of five years; this can be renewable, however, for an additional period, subject to the competitive review procedure and the availability of funds.

The Institute will attempt to maintain support for three STD program projects, dependent upon the availability of funds. For FY 1983, competition is open for support of at least two of these currently funded program projects in STD research. Although no specific level of available funding can be cited, the projects currently supported range from $271,859 to $468,313 in direct costs annually.

This program is supported under authorization of the Public Health Service Act, Public Law 78-410, as amended. The Catalog of Federal Domestic Assistance citation is Sec. 13.856, Microbiology and Infectious Diseases Research. Awards will be administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

IV. REVIEW PROCEDURES AND CRITERIA

All proposals will receive an initial peer review by the Microbiology and Infectious Diseases Advisory Committee, a chartered Institute advisory committee. Final review will be made by the National Advisory Allergy and Infectious Diseases Council; applicants will be notified following the Advisory Council meeting in May 1983. The earliest possible funding date for approved new or competing proposals, if in a fundable category, will be July 1, 1983.

The reviewing groups will evaluate the entire program project as well as each individual subproject involved, with special consideration being given to overall scientific merit of the total project and of each of the subprojects, to innovative research approaches, and to the research team concept. The expertise of each investigator and his or her past productivity, in this or in closely related research areas, will also be considered. The facilities available, including access to clinical material, will also form part of the evaluation. Finally, budget requests for each subproject and for the total program project will be carefully reviewed. Budgetary adjustments may be made by the reviewers. A priority score will be given for the overall program project application by the initial review group. Other factors in addition to the priority score, however, also may be taken into consideration for possible support of a project.

Proposals considered by the DRG and the NIAID to be not responsive to the terms outlined in this RFA will be returned to the investigator. Late submissions will be considered not responsive to this RFA. The applicant may then wish to consider revising the application and submitting it to the Division of Research Grants as a regular research grant proposal.

All policies and requirements that govern the research grant programs of the PHS-NIH will apply.

V. METHOD OF APPLYING

The NIAID information brochure of August 1978 on program project grants should be requested from NIAID staff by prospective applicants prior to preparation of an application. The development of a program project proposal is clearly detailed in this brochure. In general, applications on standard application form PHS 398 (Rev. 5/80) should include:

1. A table of contents;

2. Description of the integrated program project with rationale and justification, and description of available laboratory and clinical facilities as well as approprite patient populations;

3. Complete description of each subproject;

4. Collaborative arrangements with other departments or with other institutions, if applicable;

5. A consolidated first year budget for the total project and a first year budget for each of the subprojects and the program core; budgets for future years' support of the total project and for each subproject are to be included.

It is recommended that Institute staff be contacted by letter of intent when development of a program project grant proposal is being considered, prior to formal submission. Inquiries should be directed to:

Milton Puziss, Ph.D., Chief
Bacteriology and Virology Branch
MIDP, NIAID
National Institutes of Health
Room 738, Westwood Building
Bethesda, Maryland 20205

For purposes of identification and processing, the words SEXUALLY TRANSMITTED DISEASES PROGRAM PROJECT should be typed in item 2 on the face page of the application and a brief covering letter should be attached indicating submission is in response to this NIAID announcement.

Application kits may be obtained from the institution's business office. If not available there, they may be obtained from:

Office of Grants Inquiries
Division of Research Grants
National Institutes of Health
Room 448, Westwood Building
Bethesda, Maryland 20205

Forward the original application and six (6) copies to:

Division of Research Grants
National Institutes of Health
Room 240, Westwood Building
Bethesda, Maryland 20205

In order to alert NIAID to the submission of the proposal, please forward a copy (not the original) of the cover letter and the application face page to

Chief, Program and Project Review Branch,
NIAID
National Institutes of Health
Room 703, Westwood Building
Bethesda, Maryland 20205

PROGRAM ANNOUNCEMENT

STUDIES ON NUTRITIONAL SUPPORT OF THE PATIENT

**NATIONAL HEART, LUNG, AND BLOOD INSTITUTE
NATIONAL INSTITUTE ON AGING
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES
NATIONAL INSTITUTE OF ARTHRITIS, DIABETES, AND DIGESTIVE AND KIDNEY DISEASES
NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES**

I. BACKGROUND INFORMATION

Nutrition is the sum of the processes by which an organism assimilates and utilizes food substances. Nutrition is basically the provision of biochemical substances in the quantities and ratios that are required for normal cellular functions. When a nutrient is given parenterally rather than enterally, it must be in a form and amount that is suitable for use in the metabolic pathways of the body. For most patients, nutrition simply maintains body mass and function until other treatment modalities are given the opportunity to affect the disease. For selected patients with cancer, trauma, infection, gastrointestinal diseases, and liver, renal, and cardiovascular and pulmonary diseases, certain elderly patients, and for infants with severe gastrointestinal congenital anomalies and low birth weight newborns, provision of adequate enteral or parenteral nutrients is thought to modulate morbidity and mortality directly.

The ability to provide nutrients for patients who cannot adequately ingest, digest or absorb food has been a major technological achievement of the past 15 years. The proper application of this important new technology is only starting to be understood. We need to know more about when to institute parenteral or enteral nutrition so that we can maximize therapy and avoid its indiscriminate use which increases medical costs and patient risk and discomfort. Apart from its obvious therapeutic importance, parenteral and enteral nutrition provides a powerful research tool with which to probe and manipulate host metabolism and physiology, particularly in animal models.

II. RESEARCH GOALS AND SCOPE

The emphasis of this program announcement is upon basic and clinical research aspects of nutritional support of patients. Some examples of areas of research interest are listed below by Institute.

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

The NHLBI is seeking research applications on the impact of nutritional status on defense functions in the adult and developing lung. Resistance to pulmonary infections and prevention of muscle fatigue for patients with acute and chronic pulmonary diseases are of interest to the Division of Lung Diseases, NHLBI.

NATIONAL INSTITUTE ON AGING

The NIA provides support for biomedical, social, and behavioral research and research training in the areas of diet and nutrition (both basic and clinical) as these relate to the aging process and needs of the aged individual. Consequently, the NIA is seeking studies that focus on enteral and parenteral nutritional support in elderly patients in acute and long-term care facilities.

The elderly in these facilities may have undergone long periods of marginal nutrition prior to entering the facility. In addition, the elderly as a group are more likely than others to be on multiple and/or long-term drug therapies. Because of those possible problems together with age-associated physiological changes such as changes in gastrointestinal and kidney functions, the elderly individual may require a different type of evaluation and a different nutritional regimen than the younger individual. Among the areas of particular interest to NIA are: specification of the nutritional requirements of elderly patients, assessment of the efficacy of current enteral and parenteral therapies for elderly patients, and the development and assessment of optimum methods for meeting the nutritional requirements of elderly patients, especially in the context of multiple disorders and medications.

Other issues include: the degree to which enteral or parenteral support impinge on psychological functioning of the elderly patient, family interactions, and social participation, and development of strategies to modify psychosocial factors and supports to foster most effective functioning.

The areas listed above are examples. They are not to be all inclusive.

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

The NIAID supports research into the interaction of nutrition, infection and immunity. Malnutrition affects immunocompetence and resistance to infection, but the precise mechanisms mediating such changes must be clarified. For example, can specific nutrients be administered to modulate the rapid metabolism and growth of immunocompetent cells? Which immunological tests can be influenced by nutritional therapy in the hypercatabolic patient? In general, the underlying disease needs to be separated from the nutritional state of the patient so that the relative effect of these two parameters on the modulation of immune function can be clarified. In addition, more research is needed to elucidate the effects of infectious agents on nutrient metabolism in patients and in animal models.

NATIONAL INSTITUTE OF ARTHRITIS, DIABETES, AND DIGESTIVE AND KIDNEY DISEASES

The NIADDK supports a broad range of investigations on the nutritional support of the patient. These may be primary nutrition-centered as well as organocentric and disease-oriented studies

Nutrition-centered research includes studies on nutritional support of the patient as it affects the nutritional status of the whole individual, such as obesity, chronic renal failure/ESRD, anorexia nervosa and surgical trauma; nutritional status assessment methodologies; effect of disease stress and related conditions on nutritional requirements and the effect of nutrient intake levels on the course of specific diseases or conditions including chronic renal failure; metabolic consequences of by-passing the intestinal tract and liver in total parenteral nutrition (TPN), especially as it relates to the synthesis of "non-essential" dietary nutrients and efficiency of utilization; micronutrient requirements including vitamins and trace minerals of patients receiving TPN for extended periods; and the combined nutrient-drug management of patients.

Organocentric or disease-oriented studies on nutritional support of patients primarily involve investigations related to kidney, liver, pancreas, bone and digestive diseases. Examples of such are studies on the use of ketoacids or other amino acid analogues as a means of recycling ammonia; the effect of bowel rest and its use in the treatment of gastrointestinal diseases; effect of vitamin D metabolites and minerals in the prevention of osteoporosis and of renal osteodystrophy; and the effect of liver damage on the impairment of metabolic synthesis of dietary "non-essentials," thereby modifying the body's needs for preformed nutrients or metabolites.

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

The NICHD is seeking studies that focus on the role that nutrition plays in early development. Particular emphasis is placed on nutritional support of the low-birth-weight infant and nutritional management of certain disease states of infancy and childhood. Included are conditions such as celiac disease and other disorders of digestion and absorption; diarrheal diseases; congenital malformations of the gastrointestinal tract and inborn errors of metabolism.

Research applications are also sought that focus on: the development and function of organ systems during parenteral nutrition; the safety and efficacy of intravenous administration of nutrients; factors regulating metabolism of these nutrients; and the influence that parenteral or enteral nutrition may have on the growth and development of the immature infant.

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

The principal goal of the research program on trauma and burns of the NIGMS is to expand the basic knowledge of the body's systemic response to accidental injury, including burns, in order ultimately to improve patient care, prevent death, speed recovery, and lessen the extent of disabilities. One area of emphasis within the program relates to studies on the metabolic and nutritional response to injury.

III. MECHANISM OF SUPPORT

The mechanism of support for this program will be the grant-in-aid. The regulations (Code of Federal Regulations, Title 42, Part 52; Title 45, Part 74) and PHS policies that govern the research grant programs of the National Institutes of Health will prevail. The award of grants pursuant to this announcement is contingent upon ultimate receipt of appropriated funds for this purpose.

IV. METHOD AND CRITERIA OF REVIEW

A. Assignment of Applications: Applications will be received by the Division of Research Grants, NIH, referred to an appropriate study section for scientific review, and assigned to individual Institutes for possible funding. These decisions will be governed by normal programmatic considerations as specified in the DRG Referral Guidelines.

B. Review Procedures: Applications in response to this announcement will be reviewed on a nationwide basis in accord with the usual National Institutes of Health peer review procedures. They will first be reviewed for scientific and technical merit by a review group composed mostly of non-Federal scientific consultants (study section). Following study section review, the application will be evaluated by the appropriate Institute Advisory Council or Board with respect to the adequacy of the technical merit review and the program relevance of the research proposed. The review criteria customarily employed by the National Institutes of Health for regular research grant applications will prevail.

C. Deadlines: Applications will be accepted in accordance with the usual receipt dates for new applications: July 1, March 1, and November 1.

Investigators considering applying for program project grants should contact a representative of the appropriate Institute (see below) to obtain guidelines and instructions. Prospective applicants should note that the receipt dates for program project grant applications are June 1, October 1, and February 1.

Applications received too late for one review cycle will be held for the succeeding cycle.

V. METHOD OF APPLYING

Applications should be submitted on form PHS 398 which is available in the business or grants and contracts office at most academic and research institutions. The phrase "PREPARED IN RESPONSE TO NIH NUTRITIONAL SUPPORT PROGRAM ANNOUNCEMENT" should be typed into item 2 of the first page of the application.

The original and six copies of the application should be sent or delivered to:

Application Receipt Office
Division of Research Grants
National Institutes of Health
Room 240, Westwood Building
Bethesda, Maryland 20205

For further information, investigators are encouraged to contact one or more of the following individuals:

National Heart, Lung, and Blood Institute

Dorothy Gail, Ph.D.
Structure and Function Branch
Division of Lung Diseases
National Heart, Lung, and Blood Institute
Room 6A03, Westwood Building
Bethesda, Maryland 20205

Telephone: 301-496-7171

National Institute on Aging

Elizabeth A. McGuire, Ph.D.
Physiology of Aging Branch
Biomedical Research and Clinical Medicine
National Institute on Aging
Building 31, Room 5C-27
Bethesda, Maryland 20205

Telephone: 301-496-9350

National Institute of Allergy and Infectious Diseases

Robert Edelman, M.D.
Chief, Clinical and Epidemiological Studies Branch
Microbiology and Infectious Diseases Program
Building 31, Room 7A49
Bethesda, Maryland 20205

Telephone: 301-496-5893

National Institute of Arthritis, Diabetes, Digestive and Kidney Diseases

Gerald Combs, Ph.D.
Nutrition Program Director
Digestive Diseases and Nutrition
Room 601, Westwood Building
Bethesda, Maryland 20205

Telephone: 301-496-7823

National Institute of Child Health and Human Development

Gilman D. Grave, M.D.
Head, Nutrition and Endocrinology Section
Clinical Nutrition and Early Development Branch
Landow Building, Room 7C17
Bethesda, Maryland 20205

Telephone: 301-496-5575

National Institute of General Medical Sciences

Emilie A. Black, M.D.
Assistant Director for Clinical Research
Westwood Building, Room 925
Bethesda, Maryland 20205

Telephone: 301-496-7373

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

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NOTICE

Change in Receipt Dates for RFA-NCI-DRCCA-CCB-82-6

An announcement in the January 29, 1982 Guide for Grants and Contracts (Vol. 11, No. 2, pages 15-18) summarized a Request for Proposals (RFA) for cancer control units for defined population studies. Receipt dates for letters of intent and application deadline for that RFA have been changed from March 31, 1982 to April 30, 1982 (letter of intent) and from July 15, 1982 to August 15, 1982 for submission of applications. Applications will be reviewed by the National Cancer Advisory Board at its May, 1983 meeting, with start dates around July, 1983. Additional information and copies of the RFA may be obtained from:

Carlos E. Caban, Ph.D.
Program Director
Division of Centers, Resources
and Community Activities
National Cancer Institute
National Institutes of Health
Blair Building, Room 716B
8300 Coleville Road
Silver Spring, Maryland 20910

NOTICE

The Program Announcement "Experimental Research Related to Mammographic Screening for Human Breast Cancer" was published in the NIH Guide to Grants and Contracts, Vol. 9, No. 2, pp. 33-35, January 25, 1980. The Breast Cancer Program of the National Cancer Institute no longer considers it necessary to provide special encouragement for grant applications for animal and tissue culture studies that will provide new and relevant information on problems related to mammographic screening for human breast cancer. Cancellation of this Program Announcement does not prevent an investigator from submitting a grant related to this topic through the regular DRG mechanism.

SPECIAL EMPHASIS RESEARCH CAREER AWARD IN LABORATORY ANIMAL SCIENCE (SERCA)

ANIMAL RESOURCES PROGRAM

DIVISION OF RESEARCH RESOURCES

I. INTRODUCTION

The Division of Research Resources announces a new Special Emphasis Research Career Award in Laboratory Animal Science. This special award is made to develop multidisciplinary veterinary researchers who will direct their research toward refining the use of laboratory animals in biomedical research, the study of significant laboratory animal disease problems occurring in vivarial settings, and the development of new animal models useful in solving biomedical research problems.

This award emphasizes indepth experience for the laboratory animal specialist in various fundamental and clinical scientific disciplines. In the initial phase, the awardee is expected to develop capabilities in fundamental, applied, and/or clinical research. In the final phase, the awardee is expected to undertake a multidisciplinary research program aimed at a better understanding of a laboratory animal disease problem or development or utilization of an animal model in the solving of a biomedical research problem. This award is not intended for established investigators.

II. BACKGROUND

Laboratory animals are used in approximately 55 percent of the research projects supported by the National Institutes of Health. The SERCA is meant to stimulate the development of research on laboratory animal disease problems and the further application of these phenomena to the solving of human health research problems. Some of the opportunities available are the development of new models, the utilization of the laboratory animal diagnostic laboratories supported by DRR, and other biomedical resources, in identifying new animal models, in further defining these models, and utilization of several species which have similar diseases to develop composite models which may be useful in solving health problems.

III. OBJECTIVES OF THE AWARD

The SERCA provides opportunities for a biomedical researcher trained in laboratory animal science who wishes to develop research expertise in the broad fundamental and clinical disciplines essential for a multidisciplinary approach to research opportunities in laboratory animal science and to the utilization of laboratory animal health disorders, to the solution of human health problems.

This award is intended to:

- Encourage qualified individuals at early stages of their scientific careers to develop research interest and skill in disciplines such as laboratory animal medicine, pathology, microbiology, genetics, biochemistry, and behavioral sciences.
- Provide support for individuals to pursue a program of research in the various fundamental and clinical research disciplines related to laboratory animal sciences and animal health problems in laboratory animals, or models for human disease which may be identified by practitioners and bench scientists working with human health research problems.
- Create a pool of highly qualified laboratory animal investigators with experience and skills in the clinical and basic science disciplines necessary to develop a laboratory animal model. These investigators should possess indepth experience in their research disciplines and a breadth of knowledge in related fields of interest.

IV. PROVISIONS OF THE AWARD

The SERCA provides 5 years of support for a multidisciplinary approach to research investigation and development. Awards will be made on an annual basis, and will be contingent upon the continued availability of funds.

During the first three years of SERCA support, the awardee is expected to develop capabilities in fundamental, applied and/or clinical research related to the basic and clinical science aspects of laboratory animal science. These activities should be oriented around the initiation of a specific research project(s). Exposure to multiple disciplines, such as physiology, biochemistry, genetics, immunology, pathology, microbiology, pharmacology, nutrition and epidemiology should be included in the candidate's plans presented in the original application. Investigators are encouraged to pursue these activities in more than a single laboratory at one institution. For this developmental phase, in addition to funds for salary and fringe benefits, up to $8,000 direct costs may be requested for research support (see section B.).

During the third year of SERCA support, an application must be submitted detailing plans for an extended research program for both years four and five of the award. The expanded research program, of the awardee's own design, must focus on the basic and clinical science aspect of laboratory animal science. In addition to plans for an expanded research program, this application should summarize progress made during the first 3 years of SERCA support and should include a detailed budget for research support not to exceed $15,000 per year direct costs (in addition to the awardee's salary and fringe benefits) for the fourth and fifth years of the award. The research support budget awarded for the last two years will be determined following scientific review by DRR staff and Council. If the research support award is not favorably recommended, the continuation of salary support will be re-evaluated.

As detailed above, the SERCA grant is made annually to the awardee's parent institution for each budget period. Costs allowed may include:

A. Awardee's Salary

Up to a maximum of $30,000 from SERCA funds for salary support may be requested. In addition, fringe benefits will be provided and institutional supplementation is permitted.

B. Research Support (limited to $8,000/year for years 01 through 03 and $15,000 for years 04 and 05;

Equipment: Specialized research equipment essential to the proposed program may be requested. However, available facilities should include most of the necessary equipment;

Supplies: Consumable supplies essential to the proposed program may be requested;

Tuition for training courses: If essential to the awardee's individual training program, funds for tuition may be requested.

Other Costs: In addition, funds may also be requested for technical assistance, consultant costs, domestic travel, publication costs and other appropriate expenses which are essential to the proposed program.

C. Indirect Costs

Funds may be requested for the reimbursement of actual indirect costs at a rate of up to, but not to exceed, 8% of the total allowable direct costs of each award.

V. CRITERIA FOR ELIGIBILITY

Candidates for a Special Emphasis Research Career Award in Laboratory Animal Science must:

1. Hold a D.V.M. degree.
2. Have a minimum of two years post-D.V.M. research experience which may include one year of clinical training in the sub-specialty of laboratory animal medicine or appropriate disciplinary training.
3. Be nominated by an institution on the basis of qualifications, interests, accomplishments, motivation and potential for a research career. Evidence of the commitment of the institution to the candidate's

research development must be provided. It is not essential for the applicant institution to commit itself in the application to eventual placement of the candidate on its permanent full-time faculty, but it is expected that institutions will choose the candidates with potential for appointment at that or similar institutions.

4. Plan, with an advisor who is a mature investigator in the field at the parent institution, a developmental and research program (which may involve travel to other institutions) in which the awardee will receive development and research experience in preparation for a future career of independent research. The candidate's proposed research projects during the first three years of the award must be described.

5. Agree to inform the DRR for a period of five years subsequent to completion of the award about academic status, publications, and grants or contracts relative to the focus of this award.

6. Candidates for an award must be citizens or noncitizen nationals of the United States or its possessions and territories or must have been lawfully admitted to the United States for permanent residence at the time of application.

VI. APPLICATION

Applications must be submitted on form PHS-398, which is available at most grantee institutions, or may be obtained from the Division of Research Grants, NIH. Application receipt dates are June 1, October 1 and February 1.

Prospective applicants should contact the office listed below for supplemental instructions to be used in preparing the application, for information concerning peer review, and for inquiries related to applicant eligibility, appropriate areas of research emphasis, and SERCA program administration:

John E. Holman, D.V.M., Ph.D., Director
Laboratory Animal Sciences Program
Animal Resources Branch
Division of Research Resources
Building 31, Room 5B59
National Institutes of Health
Bethesda, Maryland 20205

Telephone: (301) 496-5175

ANNOUNCEMENT

SPECIAL EMPHASIS RESEARCH CAREER AWARD: DIABETES MELLITUS-OBSTETRICAL, PERINATAL, AND PEDIATRIC ASPECTS

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

NATIONAL INSTITUTE OF ARTHRITIS, DIABETES, DIGESTIVE AND KIDNEY DISEASES

Application Receipt Date: June 1 Annually

This is to announce the annual receipt date of June 1 for applications for the SERCA: Diabetes Mellitus - Obstetrical, Perinatal, and Pediatric Aspects. Applications received on or before June 1, 1982 should specify a project start date of July 1, 1983. The next receipt date will be June 1, 1983 for a possible start date of July 1, 1984.

The award is intended to:

- encourage qualified individuals in the early stages of their post-graduate medical and scientific careers to develop research interests and skills in the obstetrical, perinatal, and pediatric aspects of diabetes mellitus;
- provide support for individuals to pursue a program of research in various fundamental and clinical research disciplines related to diabetes mellitus during pregnancy and its associated neonatal morbidity and mortality; and
- create a pool of highly qualified investigators with experience and skills in the obstetrical, perinatal, and pediatric aspects of diabetes mellitus for a future role in research, teaching, and clinical care.

The Special Emphasis Research Career Award provides the opportunity for an obstetrician or pediatrician with developing research interests to acquire experience and skill in the broad fundamental and clinical scientific disciplines essential for a multidisciplinary approach to the endocrinologic and metabolic aspects of diabetes mellitus in obstetrical, perinatal, and/or pediatric contexts. This SERCA emphasizes in-depth experience in several fundamental and clinical scientific disciplines which are not dependent upon a single laboratory or institution.

PROVISIONS OF THE AWARD

This nonrenewable award provides support for a five-year period of full-time research and related activities. The latter may include research development activities as well as involvement in patient care to the extent that it will strengthen research skills. The SERCA grant made to the awardee's parent institution provides up to $30,000 per year for full-time salary support plus fringe benefits. A maximum of $8,000 per year during the first three years and up to $20,000 per year during the last two years will be provided for necessary research costs including technical assistance, equipment, supplies, consultant costs, domestic travel, patient care cost, publication, and other costs.

Working closely with an advisor, the candidate is expected to develop capabilities in fundamental, applied, or clinical research in the metabolic and endocrinologic aspects of diabetes in gestational, perinatal, or pediatric contexts. These activities should be design. Exposure to multiple disciplines, such as physiology, biochemistry, biophysics, pharmacology, nutrition and epidemiology should be included in the candidate's plans. Investigators are encouraged to pursue these activities in more than a single laboratory. At the completion of this five-year award, the individual should be in a position to compete in regular NIH research grant award programs.

ELIGIBILITY REQUIREMENTS

Candidates for the SERCA Award must: (1) hold an M.D. or equivalent professional degree (e.g., D.D.S., D.O., D.V.M., etc.); (2) have a minimum of three years post-M.D. experience, including one year of clinical training in obstetrics, pediatrics or endocrinology-metabolism, or two years post-M.D./Ph.D. experience or equivalent. M.D./Ph.D. applicants should possess significant experience in metabolism, endocrinology, obstetrics, pediatrics, physiology, biochemistry, pharmacology, or other relevant areas of interest, such as epidemiology; (3) be citizens or noncitizen nationals of the United States or its possessions or territories or must have been lawfully admitted to the U.S. for permanent residence at the time of application; (4) meet certain other eligibility requirements specified in the SERCA Program Guidelines (See "For Additional Information").

DEADLINE FOR RECEIPT OF APPLICATIONS

SERCA applications will be received once a year according to the following schedule:

Application Date	Council Review	Start Date
June 1	Jan/Feb*	July 1*

* of the year following application receipt.

FOR ADDITIONAL INFORMATION

Prospective applicants are encouraged to review the SERCA Guidelines which detail eligibility requirements and application procedures. In addition, prior to preparing an application, individuals are strongly encouraged to discuss their potential eligibility as well as their areas of research interest with the Program Director listed below. Requests for copies of the SERCA Guidelines as well as questions related to eligibility, etc., should be directed to:

Maureen Harris, Ph.D., M.P.H.
Acting Director, Career Development Program
National Institute of Arthritis, Diabetes,
Digestive and Kidney Diseases, NIH
Westwood Building, Room 607
Bethesda, Maryland 20205

Telephone: (301) 496-7595

ANNOUNCEMENT

SPECIAL EMPHASIS RESEARCH CAREER AWARD: DIABETES MELLITUS - CARDIOVASCULAR, METABOLIC, AND ENDOCRINOLOGIC ASPECTS

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

NATIONAL INSTITUTE OF ARTHRITIS, DIABETES, DIGESTIVE AND KIDNEY DISEASES

Application Receipt Date: June 1 annually

This is to announce the regular annual receipt date of June 1 for applications for the SERCA: Diabetes Mellitus - Cardiovascular, Metabolic, and Endocrinologic Aspects. Applications received on or before June 1, 1982 should specify a project start date of July 1, 1983. The next receipt date will be June 1, 1983 for a possible start date of July 1, 1984.

The award is intended to:

- o encourage qualified individuals in the early stages of their post-graduate medical and scientific careers to develop research interests and skills in the metabolic, endocrinologic, and cardiovascular aspects of diabetes mellitus;
- o provide support for individuals to pursue a program of research in various fundamental and clinical research disciplines related to diabetes mellitus and its sequelae, at one or more domestic institutions which offer superior opportunities in these areas; and
- o create a pool of highly qualified investigators with experience and skills in the cardiovascular, metabolic, and endocrinologic aspects of diabetes mellitus for future roles in related areas of research.

The Special Emphasis Research Career Award (SERCA) provides the opportunity for an individual with developing research interests to acquire experience and skill in the broad fundamental and clinical scientific disciplines essential for a multidisciplinary approach to the study of the metabolic, endocrinologic, and cardiovascular aspects of diabetes mellitus. This award emphasizes in-depth experience in several fundamental and clinical scientific disciplines which are not necessarily dependent upon a single laboratory institution.

PROVISIONS OF THE AWARD

This non-renewable award provides support for a five-year period of full-time research and related activities. The latter may include research development activities as well as involvement in patient care to the extent that it will strengthen research skills. The SERCA grant made to the awardee's parent institution provides up to $30,000 per year full-time salary support plus fringe benefits. A maximum of $8,000 per year during the first three years and $20,000 per year during the last two years will be provided for necessary research costs including technical assistance, equipment, supplies, consultant costs, domestic travel, patient care costs, publication, and other costs.

While working closely with an advisor, the awardee is expected to develop capabilities in fundamental, applied, and/or clinical research in the cardiovascular, metabolic, and endocrinologic aspects of diabetes. This should include exposure to multiple disciplines, such as physiology, biochemistry, biophysics, pharmacology, nutrition, and/or epidemiology. Investigators are encouraged to pursue these activities in several laboratories, and if appropriate, at more than one institution. In addition, an applicant must propose a research project of his/her own design which focuses on the cardiovascular, endocrinologic, and metabolic aspects of diabetes and which is of such scope that, within three years, evidence of independent investigative capability will be present. At the completion of this five-year award, the individual should be in a position to compete in regular NIH research grant award programs.

ELIGIBILITY REQUIREMENTS

Candidates for the SERCA Award must (1) hold an M.D. or equivalent professional degree (e.g., D.D.S., D.O., D.V.M., etc.); (2) have a minimum of three years post-M.D. experience, including one year of clinical training in the sub-specialties of either cardiovascular disease or endocrinology-metabolism, or two years post-M.D./Ph.D. experience or equivalent. M.D./Ph.D. applicants should possess significant experience in metabolic, endocrine, or related areas, cardiovascular physiology, biochemistry, pharmacology, or other relevant areas of interest, such as epidemiology; (3) be citizens or noncitizen nationals of the United States or its possessions or territories or must have been lawfully admitted to the U.S. for permanent residence at the time of application; (4) meet certain other eligibility requirements specified in the SERCA Program Guidelines.

FOR ADDITIONAL INFORMATION

Prospective applicants are encouraged to review the SERCA Guidelines which detail eligibility requirements and application procedures. In addition, prior to preparing an application, individuals are strongly encouraged to discuss their potential eligibility as well as their areas of research interest with the Program Director listed below. Requests for copies of the SERCA Guidelines as well as questions related to eligibility, etc., should be directed to:

Maureen Harris, Ph.D., M.P.H.
Acting Director, Career Development Program
National Institute of Arthritis, Diabetes,
Digestive and Kidney Diseases, NIH
Westwood Building, Room 607
Bethesda, Maryland 20205

Telephone: (301) 496-7595

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA NIH-NCI-DRCCA-82-2

THE ROLE OF NATURAL INHIBITORS IN THE PREVENTION OF CANCER

NATIONAL CANCER INSTITUTE

Application Receipt Date: June 15, 1982
Letter of Intent Receipt Date: April 30, 1982

The Division of Resources, Centers, and Community Activities, National Cancer Institute, is interested in supporting studies which are directed at examining the role of several natural inhibitors in the prevention of cancer.

The proposed studies should seek to (1) elucidate further the protective effect of several natural inhibitors in reducing the incidence of various site specific cancers, and (2) lead to a greater understanding of the extent, or action, of several natural inhibitors in the possible cancer prevention processes in humans. Clinical and epidemiological studies are being requested to develop basic information which may be helpful at a later date in decision making with regard to the application of the compounds in clinical trials for chemoprevention.

Grants may be awarded to profit and nonprofit organizations and institutions, governments and their agencies, and occasionally to individuals. This type of grant solicitation (the RFA) is utilized when it is desired to encourage investigator-initiated research projects in areas of special importance to the National Cancer Program. Applicants funded under the RFA are supported through the customary NIH grant-in-aid, in accordance with PHS policies applicable to Research Project Grants, including cost sharing. However, the RFA solicitation represents a single competition, with a specified deadline for receipt of applications. All applications received in response to the RFA will be reviewed by the same National Institutes of Health (NIH) Initial Review Group.

The present RFA announcement is for a single competition with a specified deadline of June 15, 1982 for receipt of applications. Applications should be prepared and submitted in accordance with the aims and requirements described in the following sections:

I. BACKGROUND

Chemoprevention refers to the intake or use of chemical agents to interrupt a sequence of events leading to malignancy, or that follow the exposure of an individual to carcinogenic agents which may result in the development of malignancy. A number of natural inhibitors including vitamin C, beta carotene, vitamin A or its analogs, selenium and alpha tocopherol have been associated, in animals or test systems, with the inhibition of carcinogenesis or have been

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This program is described in the Catalog of Federal Domestic Assistance number 13.393, Cancer Cause and Prevention Research. Awards are under authorization of the Public Health Service Act, Section 301(c) and Section 402 (Public Law 78-410, as amended; 42 USC 241; 42 USC 282) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

associated with reduced cancer incidence, in epidemiological investigations. A number of mechanisms have been postulated including increased detoxification of the carcinogen, alteration of metabolism by decreased activation, scavenging of the active molecular species, prevention of the carcinogenic agent from reaching the critical target in the cell, altering permeability or transport, and competitive inhibition.

Because of the numerous reports concerning the effectiveness of these compounds in interfering with carcinogenesis in animals and the many epidemiological studies suggesting a possible negative association of them with cancer incidence, especially in dietary factors and nutrition studies, this RFA is announced.

II. OBJECTIVES AND SCOPE

The purpose of this RFA is to solicit applications from qualified investigators interested in furthering the understanding of the role of beta carotene, vitamin A or analogs, vitamin C, selenium and alpha tocopherol in the prevention of cancer.

The studies envisioned include, but are not necessarily limited to, the following approaches:

(1) a. Case Control Studies - utilizing cancer patients and suitable matched controls to study the possible relationship of the designated inhibitors with cancer incidence. Measurement of inhibitor intake or levels should be as direct as possible; indices not specific for these inhibitors will not be considered for the RFA. These studies may also include investigation of appropriate biological indicators such as serum markers, enzyme levels, etc.

b. Alternate approaches would involve the study of existing data bases with accurate intake information on the designated compounds and the subsequent prospective study of the development of cancer in a defined population.

(2) Cohort Studies - involving a population which has consumed varying levels of the designated inhibitors. The investigator would subsequently determine the relative risks of cancer incidence through follow-up of the population over a number of years. Examination of appropriate biological indicators of intake are also desired.

(3) Safety and Adverse Health Effects Studies - Human studies examining the long-term consequence of chronic intake of various compounds to monitor for possible adverse health effects. These studies would be initiated in defined populations identified as having high intake levels of the inhibitors. Approaches might be either case control or cohort studies. Wherever possible, collection and assessment of these data should be incorporated into the studies listed in (1) or (2). Understandings gained through these investigations would also be valuable in examining the feasibility of conducting clinical trials.

(4) Risk Reduction Clinical Trials - A fourth category of interest involves populations known to be at very high risk but free of neoplasia, or high risk with identified precursory or pre-cancerous lesions. These studies would require the administration of the designated natural inhibitors in a

randomized study with follow-up to determine the effect of the compound. Proposals involving studies of populations already having neoplastic lesions are not acceptable within the scope of this RFA, but may be submitted in accordance with appropriate grant guidelines and may be of interest to other components of the NCI; such proposals would not be responsive to this RFA, however, and would be handled through the usual grant-review process.

Several items with regard to the proposal itself are provided as follows:

(1) The applicant is encouraged, where germane, to focus attention on a specific target group, or to identify a source of data, and to address the methodological, organizational, and theoretical issues in a detailed manner.

(2) The applicant should provide a description of the target or population group chosen and should justify the selection of this group. The group should be specified, where appropriate, by age, sex, race, socio-economic status, dietary customs, education, location, occupational or life style risk factors, and relevancy to a specific cancer problem and to its possible prevention by the designated inhibitors.

(3) The applicant should specify the source of data and should document its availability and any required cooperation. If possible, the applicant is encouraged to draw upon existing data rather than collection of extensive original data.

(4) Successful grant awardees under this RFA will be required to cooperate with the National Cancer Institute in the evaluation of the role of these designated inhibitors in cancer prevention. A program meeting of one or two days' duration will be held in Bethesda each year of the program in order to review and assess overall progress. Proposals should contain a statement that awardees will participate in this aspect of the program and proposals should include sufficient travel funds within the budget to accommodate expenses for one or two participants at this annual project meeting.

III. MECHANISM OF SUPPORT

This RFA will use the traditional National Institutes of Health grant-in-aid. Responsibility for the planning, direction and execution of the proposed research will be solely that of the applicant. The total project period for applications submitted in response to the present RFA should not exceed three years. The intent is to fund at least six projects, with total costs amounting to approximately $2.0 million for the first year. This level of activity is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of the National Cancer Institute, the award of grants pursuant to this RFA is also contingent upon the continuing availability of funds for this purpose.

IV. REVIEW PROCEDURES AND CRITERIA

A. Review Method

Each application submitted in response to the RFA will be reviewed by: (1) an appropriate review panel of the National Institutes of Health, and (2) the National Cancer Advisory Board at one of its scheduled quarterly meetings. All applications will be evaluated on a competitive basis.

B. Review Criteria

Applications must be responsive to this RFA, in the sense of being directed towards the attainment of the stated programmatic goals and fall within one or more of the specified research categories (see II. OBJECTIVES AND SCOPE). If the application is judged by the National Cancer Institute to be not responsive, the applicant will have the opportunity of having the application considered along with other unsolicited proposals received by the National Institutes of Health in the review cycle which is current at that time.

The factors considered in evaluating each response to this RFA will be:

1. Scientific merit of the research approach, design, and methodology.
2. Scientific, technical, or medical significance and originality of the proposed research.
3. Research experience and/or competence of the Principal Investigator and staff to conduct the proposed studies.
4. Adequacy of time (effort) which the Principal Investigator and staff would devote to the proposed studies.
5. Relevancy and appropriateness of the specific target population along with assurance as to their accessibility.
6. Identity of sources of data, tissues, fluids, etc., procedures for their analysis and assurances as to their accessibility.
7. A willingness to work cooperatively with other projects of a similar nature and with the NCI on the project.
8. Reasonableness of the proposed budget and duration.

V. METHOD OF APPLYING

A. Letter of Intent

Prospective applicants are asked to submit a one-page letter of intent which includes a very brief synopsis of proposed areas of research and identification of any other participating institutions. This letter should be sent to Dr. Malone at the address located under VI.

The Institute requests such letters only to provide an indication of the number and the scope of applications to be received. The letter of intent is not binding; it will not enter into the review of any proposal subsequently submitted nor is it a necessary requirement for application.

B. Format of Application

Applications must be submitted on Form PHS 398, the application form for research project grants. Application kits are available at most institutional business offices, or may be obtained from the Division of Research Grants, NIH. The conventional presentation format and details applicable to regular research grant applications should be followed, and the requirements specified under Review Criteria (IV.B.) must be fulfilled. The words "PROPOSAL IN RESPONSE TO RFA NIH-NCI-DRCCA-82-2, STUDIES TO EXAMINE THE ROLE OF NATURAL INHIBITORS IN THE PREVENTION OF CANCER," must be typed in bold letters across the top of the face page of the application.

C. Application Procedures

The completed original application and six (6) copies should be sent or delivered to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205

To ensure their review, applications should be received by June 15, 1982. Applications received after that date will not be considered under this RFA, but the applicant will have the opportunity of having them considered in the next regular grant review cycle. Also, the Division of Research Grants (DRG) will not accept any application in response to this announcement, that is the same as one currently being considered by any other NIH awarding unit. A copy of the application should also be sent to Dr. Malone at the address shown below.

VI. INQUIRIES

Inquiries may be directed to:

Winfred F. Malone, Ph.D., M.P.H.
Preventive Medicine Branch
Blair Building - Room 624
National Cancer Institute
Bethesda, Maryland 20205

Telephone: (301) 427-8648

REQUEST FOR RESEARCH GRANT APPLICATION: RFA

NIH-NIAID 82-6

PROGRAM PROJECTS IN TRANSPLANTATION IMMUNOLOGY

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Application Receipt Date: August 2, 1982

The National Institute of Allergy and Infectious Diseases (NIAID) invites applications for program project grants, to be initiated during FY 1983, to conduct investigations of the immune system in human recipients of allografts.

BACKGROUND INFORMATION

The Genetics and Transplantation Biology Branch of the Immunology, Allergic and Immunologic Diseases Program of the NIAID sponsors basic and applied research in immunogenetics and transplantation immunology through grants and contracts, and by providing cells and reagents for histocompatibility testing. This request for applications (RFA) is intended to stimulate the formulation of collaborative, coordinated approaches, involving transplant clinicians and basic immunologists, to the clarification and manipulation of the immune processes that determine acceptance or rejection of allografts.

The practice of transplantation has evolved to the point that the technical aspects of the surgery are not limiting. The major remaining hazards are associated with rejection and with the immunosuppressive therapy employed to prevent or control it. In immunology, momentous advances in technical procedures and in the understanding of molecular and cellular processes have been made very recently. The major new tools available to immunologists include cell culture and propagation techniques, monoclonal antibodies of exquisite specificity produced by cell hybridization, and techniques of genetic analysis and manipulation at the molecular level. The major conceptual advances are centered on the clarification of the complex regulatory mechanisms involving soluble factors and interactions among specialized cell populations. Transplant recipients subjected to manipulation of their immune system both by means of the immunosuppressive therapy and by the graft itself constitute a unique resource in which a large range of procedures is already accepted practice. They, therefore, offer a superb opportunity to basic immunologists for the investigation of the human immune system subjected to deliberate disturbances. In turn, the guidance to the clinician that will result from the understanding of the immunological events that transpire in connection with transplantation and its treatment and from the elucidation of the mechanisms that connect and control these events should prove invaluable.

This program is described in the Catalog of Federal Domestic Assistance No. 13.855, Immunology, Allergic and Immunologic Diseases Research. Awards will be made under the authroity of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulation 42 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

RESEARCH GOALS AND SCOPE

1. The program project grant is awarded to an institution on behalf of a program project director for the support of a broadly based but highly integrated long-term research program. It is anticipated that ultimately several awards will be made for work focused on organ and tissue transplantation. The beginning date of the awards is expected to be April 1, 1983 and their terms are up to five years.

2. Support, under the program project grant, will be available for the acquisition of resources necessary for the conduct of the scientific studies (salaries, equipment, supplies, etc.) and for such development of research procedures as will render them useful in a clinical setting. Support will not be provided for other non-research activities such as routine patient care or continuing medical education.

3. Applications should heavily emphasize collaboration in research between transplant clinicians and immunologists, and the application of the most up-to-date concepts and techniques of immunology to the evaluation of the immune system of the recipients in all circumstances attendant to the transplantation.

   The application should be a multidisciplinary research program that has a well defined central research focus or objective. As with other program projects, the individual projects of which they consist should be interrelated, all contributing to the program objective.

4. The objectives of the research should be (a) the clarification of the status of the immune system, specifically of the immunoregulatory balance (1) prior to transplantation in its relatively normal state or, if the transplant is occasioned by a disturbance of the immune state, in the causative disordered state, (2) in the course of preparation for the transplant whose objective is the reduction of responsiveness (immunosuppression) or the induction of tolerance, (3) postoperatively during maintenance immunosuppression as the graft becomes established, (4) during rejection episodes, and (5) during treatment of rejection, and (B) the modulation of immunological activity on the basis of the information so obtained.

5. Appropriate approaches may include but are not restricted to investigations of:

   (a) cellular regulatory interactions among the lymphocyte subpopulations

   (b) modulation of immune activity by soluble factors, including antibodies specific for lymphocyte subsets and antiidiotype antibodies

   (c) effects of chemical and physical agents used for immunosuppression of the metabolic processes and, overall, on the physiological functions of the lymphocytes of patients

  (d) cell cloning and molecular genetic manipulations of lymphocytes whose objective is the production of cells with properties of use in therapeutic procedures

6. The investigations should center on human subjects and may deal with cells of the immune system maintained and/or propagated in vitro. Such studies on animal models may be undertaken as will provide direct guidance for the planning and conduct of the clinical investigations.

7. Designation of the Program Project Director should be based upon accomplishment, experience as a senior scientist, and ability to assume leadership of the investigative group and responsibility for scientific, professional and administrative functions. A substantial commitment of time is expected. Leaders of individual projects should have demonstrated a substantial record of accomplishment in transplantation and/or immunology.

MECHANISM OF SUPPORT

In FY 83 NIAID plans to award at least one Program Project in Transplantation Immunology, contingent upon the availability of funds. Support of the Program project(s) will be limited to a maximum of five years. Funding beyond the first year will be contingent on satisfactory progress and availability of funds. Consideration of renewal will be subject to reissuance of this RFA.

The receipt date for applications will be August 2, 1982. They will undergo initial review in November 1982 by the Transplantation Biology and Immunology Subcommittee of the Allergy, Immunology and Transplantation Committee and secondary review by the NIAID Advisory Council in January, 1983. April 1, 1983 will be the earliest starting date for successful applications.

Grant funds may be utilized to support the reserch activities of scientific and professional personnel, administration, consultation services, central support services, equipment, supplies, travel, and publication costs. Support for research-related costs of patient involvement may be authorized. Since the program cannot provide funds for new construction, adequate physical facilities must be available for the primary needs of the project. However, moderate alterations or renovations to enhance clinical or laboratory facilities may be allowed if they are necessary to meet objectives of the proposed program.

PROCEDURES AND CRITERIA

Applications assigned to the NIAID will be reviewed initially by the Transplantation Biology and Immunology Subcommittee of the Allergy, Immunology and Transplantation Research Committee, managed by the Program and Project Review Branch, Extramural Activities Program, NIAID.

The steps in the review process may, but need not, include a project site visit to evaluate the overall merit of the application.

Review Criteria:

Review criteria include evaluation of the following, not necessarily in order of importance:

- The scientific merit and significance of the overall program goals and the development of a well-defined central research focus.

- The cohesiveness and multidisciplinary or multifaceted scope of the program.

- The leadership, scientific ability, and administrative competence of the Program Project Director and his or her commitment and ability to devote substantial time and effort to the program.

- The qualifications, experience, and commitment of the collaborating investigators responsible for the various aspects of the program including their ability to devote adequate time and effort to the program.

- The academic and physical environment in which the research will be conducted, including the availability of space, equipment, patients, and the potential for interaction with active scientists from other departments and/or institutions.

- A sound administrative and organizational structure that facilitates attainment of the objective(s) of the program.

- Arrangements for internal quality control of on-going research, allocation of funds, day-to-day management, internal communications and cooperation among the investigators involved in the program, contractual agreements, and replacement of the Program Project Director, if required, on an interim of permanent basis.

- The institutional strength, stability, and commitment to research and to the program, including fiscal responsibility and management capability to assist the Program Project Director and staff in following NIH/PHS policy.

- The appropriateness of the period of support and budget requested in relation to the proposed program.

Review by the National Allergy and Infectious Diseases Advisory Council:

The final review will be conducted by the National Allergy and Infectious Diseases Advisory Council. Factors that will be considered in this review include:

- Results of the initial scientific and technical merit review.

- Significance to NIAID program goals.

- National needs and program balance.

- Policy and budgetary considerations.

LETTER OF INTENT

Prospective program directors are encouraged to submit a "Letter of Intent" for preliminary screening by NIAID staff.

Letter of Intent should cover the following points:

1. A brief description of each of the individual projects and a brief discussion of how these projects will be interrelated.
2. A description of available laboratory facilities.
3. Ongoing basic and clinical research relating to transplantation and immunology, identifying existing projects and sources of support.
4. Past research by members of the proposed investigative group in transplantation and immunology.
5. A description of all clinical facilities available for use by the proposed project.
6. Specific information on the institution's present relevant patient load and projections for patient involvement in clinical investigation.
7. The academic positions and major research interests of the program director and his professional staff who will be involved in the work of the program project.

Letters of intent are due no later than April 30, 1982, and upon receipt will be screened by NIAID staff to determine the eligibility and suitability of the projected proposals.

Inquiries and letters should be directed to:

Henry Krakauer, M.D., Ph.D.
Chief, Genetics and Transplantation
Biology Branch
Immunology Allergic and Immunologic
Diseases Program
National Institute of Allergy and
Infectious Diseases
Westwood Building, Room 752
5333 Westbard Avenue
Bethesda, Maryland 20205

Telephone: (301) 496-7551

CONSEQUENCES OF LACK OF RESPONSIVENESS TO THE RFA OR LATE SUBMISSION

Based upon the Letter of Intent, potential applicants will be promptly advised whether or not their proposal is found to be within the research goals and scope of the program as defined in this RFA. Applicants will then have an opportunity to correct deficiencies or weaknesses and to restructure their submissions accordingly. Formal applications that are not responsive to the RFA or are not received by August 2, 1982 will not be accepted for review and will be returned to the applicant.

METHOD OF APPLYING

Before preparing an application, the prospective applicant should request a copy of the NIAID Information Brochure on Program Projects from:

Dr. Nirmal Das
Executive Secretary
Allergy, Immunology and Transplantation
Research Committee
National Institute of Allergy and
Infectious Diseases
National Institutes of Health
Westwood Building, Room 706
5333 Westbard Avenue
Bethesda, Maryland 20205

Telephone: (301) 496-7966

In order to assure adequate review it is important to follow instructions in the Information Brochure, which contains details on the format and requirements for multidisciplinary grant applications.

Use the standard research grant appliction form PHS 398 (Rev. 5/80), available in most institutional business offices or from the Division of Research Grants, NIH. In addition to following accompanying format instruction for the development of the application, include expanded material listed above under the eight points for the "Letter of Intent" and other additional information as outlined in the Information Brochure. For purposes of identification and processing, the YES box in item 2 of the face page of the application should be marked and the words Program Project in Transplantation Immunology should be typed. A brief covering letter should be attached indicating submission is in response to this NIAID announcement.

Forward to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
Bethesda, Maryland 20205

Please forward a copy (not the original) of the cover letter and the application to: (1) Dr. Henry Krakauer in order to alert NIAID to the submission of the proposal, and (2) the Chief, Program and Project Review Branch, NIAID, Room 703, Westwood Building, National Institutes of Health, Bethesda, Maryland 20205.

ANNOUNCEMENT

CLINICAL INVESTIGATOR AWARD

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Application Receipt Date: August 2, 1982
(August 1 annually thereafter)

PURPOSE

The National Heart, Lung, and Blood Institute (NHLBI) announces the availability of Clinical Investigator Awards. The clinical investigator award program is intended to:

- encourage newly trained clinicians to develop clinical and basic research interests and skills in the areas of cardiovascular, pulmonary, or blood diseases and the blood banking sciences;
- increase the pool of physician investigators in the areas of cardiovascular, pulmonary, or blood diseases and the blood banking sciences.

These awards provide the opportunity for clinically trained physicians with a commitment to research to develop into independent biomedical research investigators.

The award will enable candidates to undertake up to five years of special study and supervised experience tailored to individual needs with a sponsor (or sponsors) competent to provide research guidance. This award is intended to cover the transition between postdoctoral experience and a career in independent investigation. The clinical investigator award differs from the NIH Research Career Development Award (RCDA) in that it seeks to develop research ability in individuals with a clinical background early in the candidate's career rather than to promote the further development of research skills of individuals already demonstrating significant research achievement.

BACKGROUND

Despite a recent decline in the death rate from coronary heart disease, cardiovascular disease continues to be the number one cause of death in the United States. Arteriosclerosis and hypertension account for almost one million deaths annually. An estimated 40 million Americans have diseases of the heart and blood vessels, resulting in a large burden of acute and chronic illness and disability. Heart and blood vessel diseases cost the economy more than $50 billion per year in wages, lost productivity, and expenses for medical care.

This program is described in the Catalog of Federal Domestic Assistance Nos. 13.837, 13.838, and 13.839. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

Diseases of the lung constitute a major national health problem. An estimated 10 million Americans, both young and old, are currently affected by these diseases with an annual estimated cost to the nation of over $17 billion. In the newborn, the most common cause of death is neonatal respiratory distress syndrome. Neonatal RDS is implicated in the development of adult respiratory diseases as well. Fibrotic and immunologic lung diseases are major causes of lung problems in the young adult and may cause chronic obstructive pulmonary diseases. Of the adult respiratory diseases, emphysema and chronic bronchitis are the major causes of death.

Asthma, emphysema and chronic bronchitis represent particularly pressing health problems, since the death rate and prevalence of these conditions have increased at an alarming rate over the past 15 years. As a disabling disease, emphysema is the third leading cause of worker retirement on Social Security disability payments.

Diseases of the blood underlie, or are critical contributors to, many disorders affecting mankind. As a consequence, they are major causes of death and disability in the United States. Nevertheless no valid estimate of their adverse economic impact can be realistically made since disorders of the blood not only affect the blood itself, but all the organs and tissues through which it flows. Platelet and clotting disorders affect large numbers of individuals suffering from hemorrhagic or thrombotic episodes. Significant segments of the population have sickle cell disease, Cooley's anemia, or other hemolytic disorders. Anemias due to other mechanisms affect smaller numbers of patients. Furthermore, it is difficult to estimate the economic consequences of an inadequate blood banking and blood resource system, since the supply and management of blood and blood products underlie much routine and emergency medical practice.

The clinical investigator award program is designed to encourage recently trained physicians to develop their clinical and basic resource interests and research capabilities in heart, lung, or blood disease* areas. To help support the transition from clinical training status to that of a productive research investigator, the clinical investigator award will provide early support for clinicians with potential for developing into independent researchers.

IMPLEMENTATION

Beginning in Fiscal Year 1980, under the authorizations in Public Health Service Act, Section 301(c) and Section 413(a), the National Heart, Lung, and Blood Institute has funded clinical investigator awards. Each grant has a duration of five years and is non-renewable. Funding beyond the first year of the grant is contingent on satisfactory progress during the preceding year.

The status of the clinical investigator award program will be reviewed four years from the date of the first awards to determine whether the program should be continued. In addition, to assess the effectiveness of the program in fulfilling its objectives, the Institute intends, after completion of each grant, to follow the progress of the recipient for a period of five years to determine: (1) the investigator's professional affiliation(s),

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* The term "blood diseases" covers research into many aspects of bone marrow function and disorders of the red cell, megakaryocyte, platelet, and coagulation systems. Research on disorders of white cells, including the leukemias and other blood malignancies, and basic immunology related to the lymphoid system are the responsibility of other Institutes of the NIH and therefore cannot be supported through this mechanism.

(2) his/her record of subsequent grant or contract support, and (3) his/her record of scientific publications. It is anticipated that the experience and results achieved by the awardee from this special grant program, in the majority of cases, will provide the basis for successful competition in the regular research support programs of the Institute.
The receipt date for applications will be **August 2, 1982** and on August 1 each year thereafter. They will be evaluated by an initial review group and by the National Heart, Lung, and Blood Advisory Council. The earliest start date for successful applications will be July 1, 1983.

PROVISIONS OF THE AWARD

The clinical investigator awardee will be supported for a maximum of five years. All funds must be used to support the original awardee. Support is based on a full-time, twelve-month appointment. The awardee will be provided salary support of up to $25,000 in the first year with subsequent years up to a ceiling of $30,000, plus fringe benefits. The actual salary must be consistent with the established salary structure of the institution for persons of equivalent qualifications, experience, and rank.

Up to a total of $10,000 annually may be provided for supplies, equipment, travel, etc., which are necessary for pursuit of the awardee's research program. An appropriate sponsor must assume responsibility and provide guidance for the development of the candidate's research program.

Institutions may apply for awards on behalf of named individuals meeting the criteria for this award. Evidence of the commitment of the institution and sponsors to the candidate's research and career development is to be included in the application.

The grant will be made annually to the awardee's parent institution for each of the five annual budget periods. Costs allowed may include:

1. Awardee's Salary

   Up to a maximum of $25,000 in the first year with subsequent years up to a ceiling of $30,000 for full-ime support; in addition, fringe benefits will be provided. Institutional supplementation is permitted.

2. Research Support

   Up to a maximum of $10,000 per year.

   - Equipment: specialized research equipment essential to the proposed program. The available facilities should include most of the necessary equipmnent;
   - Supplies: consumable supplies essential to the proposed program;
   - Travel: domestic travel essential to the proposed program;
   - Tuition for training courses: if essential to the awardee's individual research development program; and
   - Other: publication costs, patient costs, etc., necessary for the research program.

3. Indirect Costs

Funds will be provided for the reimbursement of actual indirect costs at a rate up to, but not exceeding, 8 percent of the total direct costs of each award, exclusive of tuition, fees, and expenditures for equipment.

ELIGIBILITY

1. The award is designed to provide intensive, supervised research experience for clinicians. Thus, candidates are restricted to those holding health-professional degrees in the clinical sciences (M.D., D.O., or equivalent). Candidates ordinarily will have completed their clinical experience by the time the award can be made. Ordinarily a candidate in the following categories will not qualify:

   a) with more than 6 years of postdoctoral experience at the time of award;

   b) with previous independent NIH research support or its equivalent;

   c) with less than three years total postdoctoral clinical experience at the time of the award.

   In exceptional circumstances, individuals in one or more of the above categories may qualify for the award. However, the applicant must provide sufficient justification for such an exception.

   Candidates should have broad clinical training, should demonstrate individual competence in clinical activities, and should show research potential in the chosen area of interest. Candidates must provide evidence of a serious intent for research and academic careers.

2. Applicants for a Clinical Investigator Award may not submit a concurrent applicaion for an NIH Research Career Development Award, Academic Award, or for a New Investigator Research Award. A Clinical Investigator Awardee may subsequently apply for a research project grant.

3. The grantee institution must be a domestic university, medical school, or comparable institution with strong, well-established research and training programs, adequate numbers of highly trained faculty in clinical and basic science departments, and commitment and capability to provide guidance to clinically oriented individuals in the development of independent research careers.

   Candidates must be nominated by an institution on the basis of qualifications, interests, accomplishments, motivation, and potential for a research career. Evidence of the commitment of the institution to the candidate's research and development must be provided.

4. Candidates must have one or more sponsors or advisors who are recognized as accomplished investigators in the research proposed at the applicant's institution. The sponsor must provide: a) his/her concept of a development

and research plan for the awardee; b) his/her curriculum vitae (updated) with complete bibliography and research support; and c) a letter indicating his/her evaluation of the proposed awardee and his/her willingness to provide guidance and support.

5. Candidates must provide a description of the proposed research and career development plan for the five-year period of the award. The candidate must be prepared to commit full-time effort to the objectives of this award. It is required that a minimum of 75 percent effort be devoted to the research program. The balance of effort can be devoted to other clinical and teaching pursuits only if they are consonant with the program goals, i.e., the awardee's development into an independent biomedical research investigator.

6. Awardees and their sponsors will be required to submit a special, detailed progress report at the end of the third year of support. This report is to contain specific information concerning progress and accomplishments and, in particular, an appropriately detailed research plan and protocol.

7. Candidates must agree to inform the National Heart, Lung, and Blood Institute annually for a period of five years subsequent to completion of the award about academic status, publications, and research grants or contracts received.

8. Candidates for an award must be citizens or non-citizen nationals of the United States or its possessions and territories or must have been lawfully admitted to the United States for permanent residence at the time of application.

APPLICATION

Applications must be submitted on form PHS 398 which is available at the grantee institution. The original and six (6) copies of the application should be clearly labeled "NHLBI CLINICAL INVESTIGATOR AWARD PROGRAM."

The chairperson of the department sponsoring the candidate should submit, a signed statement, as part of the application, detailing the department's commitment to the candidate.

Completed grant applications should be mailed to the following address:

Division of Research Grants
National Institutes of Health
Bethesda, Maryland 20205

Upon receipt of each application at NIH, a postal card acknowledging receipt will be mailed to the applicant.

The applicant should ask three present or former supervisors or preceptor to send a letter to the Review Branch, Division of Extramural Affairs, NHLBI, attesting to his/her potential for conducting independent research. The applicant is responsible for making necessary arrangements to ensure that the reference letters are mailed by the supervisors/preceptors directly to the Review Branch.

Applications for this award are due **August 2, 1982.** The earliest start date for awards is July 1, 1983.

Subsequent competitions will occur on a once-a-year basis and the receipt dates will be August 1 of each year.

REVIEW CRITERIA

Applications for clinical investigator awards will undergo initial merit review in the Review Branch, Division of Extramural Affairs, NHLBI. Secondary review will be by the National Heart, Lung, and Blood Advisory Council. Criteria for review include:

- The candidate's potential for a career in independent research;
- The candidate's commitment to a research career;
- The eligibility of the candidate as defined in the program announcement;
- The overall merit of the candidate's five-year plan for research and the development of research skills;
- The quality of the candidate's clinical training and experience;
- The institution's ability to provide quality facilities, resources, and opportunities necessary to the candidate's research development;
- Presence of highly trained faculty in clinical and basic science departments relative to the area of study; and
- The ability and plans of the sponsor (or sponsors) who will provide the candidate with the guidance necessary for career development in research.

NHLBI STAFF CONTACTS

Inquiries about the program should be directed to:

Research Training and Development Officer
DIVISION OF BLOOD DISEASES AND RESOURCES
National Heart, Lung, and Blood Institute
Federal Building, Room 514A
Bethesda, Maryland 20205

Telehone: (301) 496-1817

Research Training and Development Officer
DIVISION OF HEART AND VASCULAR DISEASES
National Heart, Lung, and Blood Institute
Federal Building, Room 3A-08
Bethesda, Maryland 20205

Telephone: (301) 496-1724

Research Training and Development Officer
DIVISION OF LUNG DISEASES
National Heart, Lung, and Blood Institute
Westwood Building, Room 6A-05
Bethesda, Maryland 20205

Telephone: (301) 496-7668

Letters of reference and inquiries regarding review procedures should be directed to:

Dr. Carol Letendre, Executive Secretary
Research Manpower Review Committee
National Heart, Lung, and Blood Institute
Westwood Building, Room 548
5333 Westbard Avenue
Bethesda, Maryland 20205

Telephone: (301) 496-7363

ANNOUNCEMENT

CANCER CONTROL SCIENCE PROGRAM

NATIONAL CANCER INSTITUTE

I. BACKGROUND AND GOALS

The Cancer Control Program of the National Cancer Institute (NCI) is located within the Division of Resources, Centers and Community Activities (DRCCA). DRCCA has recently described the new Cancer Control Program directions, emphasizing more cancer control research, in a "Statement on Cancer Control" which was adopted in January 1981.

The Division of Resources, Centers and Community Activities, NCI, invites grant applications from interested investigators for the support of Cancer Control Science Programs. These programs will provide a scientific focus within which investigators can conduct a variety of cancer control research studies.

This "Cancer Control Science Program," together with the "Cancer Control Research Units for Defined Population Studies" program, replace the Outreach Program described in the June 1976 "Grant Guidelines to Cancer Centers for Community Outreach Programs," and the "Cancer Control Developmental and Support Grants" described therein. (The availability of a Request for Applications for a single competition for Cancer Control Research Units for Defined Population Studies was announced in the January 29, 1982 issue of the Guide. Copies of RFA-NCI-DRCCA-CCB-82-6 may be obtained from the staff contact listed at the end of this announcement.)

II. CANCER CONTROL RESEARCH

Cancer control research includes both prevention (primary and secondary) and management (diagnosis, pre-treatment evaluation, treatment, rehabilitation, and continuing care). It builds on the research and knowledge bases of epidemiological, biomedical, clinical, behavioral and other sciences. It requires carefully designed investigations, often including both study and control groups and/or defined denominator populations.

This program is described in the Catalog of Federal Domestic Assistance No. 13.399, Cancer Control. Awards will be made under the authority of the Public Health Service Act, Title IV, Section 403 (Public Law 78-410, as amended; 42 USC 284) and administered under PHS grant policies and Federal regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse of Health Systems Agency review.

The "Statement on Cancer Control," which sets forth the general scope and definition of cancer control research, states, in part:

> "The goal of a cancer control program is to reduce cancer incidence, morbidity, and/or mortality by:
>
> 1) identifying approaches that might accomplish this and performing research in defined populations to determine which are effective,
>
> 2) selective promotion and evaluation of these approaches, and
>
> 3) selective education and information dissemination for health professionals and/or the public.

The scope of cancer control includes prevention, screening, diagnosis, pretreatment evaluation, treatment, rehabilitation, and continuing care activities.

The national cancer effort includes both research into and application of control methods. These are complementary and not antagonistic activities and are part of an ordered sequence, as indicated in the following statement adapted by the Board of Scientific Counselors from the report of the President's Biomedical Research Panel.

> 'The continuum from the discovery of new knowledge to the application of such knowledge in health care includes a number of steps:
>
> 1. discovery, through research, of new knowledge and the relating of new knowledge to the existing base;
>
> 2. translation of new knowledge, through applied research, into new technology and strategy for movement of discovery into health care;
>
> 3. validation of new technology through clinical trials in defined populations, and in other ways;
>
> 4. determination of the safety and efficacy of new technology for wide-spread dissemination through demonstration projects;
>
> 5. education of the professional community in proper use of the new technology and of the lay community on the nature of these developments; and
>
> 6. skillful and balanced application of the new developments to the populations.'

Cancer control includes 2 through 5, although different relative emphasis may be placed on each of those points depending on the specific cancer and whether prevention or treatment efforts are involved.

Control and research must be mutually reinforcing and only the coordinated planning and implementation of research and control strategies will assure maximum yield from the dollars invested, maximum quality for the activities supported, and maximum, probability that the research effort will continue to provide advance suitable for future application in the control of cancer.

Cancer control should support three types of activities in defined populations:

1. research to determine how, whether and to what extent, actions proposed for a particular cancer are effective;

2. research to determine the optimal strategies for promoting actions proved efficacious for particular cancers; and

3. selective implementation of those promotional strategies proven efficacious for particular cancers.

Cancer control efforts should give highest priority to cancers meeting more than one of the following criteria:

1. cancers causing the greatest mortality/morbidity in the United States;

2. cancers for which substantial risk of cancer has been associated with common exposures...(added for this CCSP announcement);

3. cancers for which apparently effective actions are available.

The development of an effective national program for cancer control requires qualified personnel, particularly with training and experience in the disciplines of epidemiology, biostatistics, and disease control administration, and the placement of these individuals in responsible positions."

III. PHASES OF CANCER CONTROL RESEARCH

The Division of Resources, Center, and Community Activities is testing the idea of categorizing cancer control research studies into phases. Applicants are asked to classify each research project as Phase I, II, III, IV, or V as noted in the table below, and also as prevention (primary and secondary) or management (diagnosis, pretreatment evaluation, treatment, rehabilitation and continuing care). If a study does not fit this classification, the reasons it does not fit should be described.

TYPE OF CANCER CONTROL STUDY

Phase	Phase Title/Description	Prevention	Management
Phase I	Hypothesis Development		
Phase II	Research on Study Components or Methods Needed to Test the Hypothesis		
Phase III	Case-Control Studies and Other Controlled Studies Which Are Not Defined Population Studies		
Phase IV	Defined Population Studies		
Phase V	Demonstration and Implementation Studies		

Definitions

Phase I.
Hypothesis Development

Development of cancer control hypotheses of which control measures, approaches, or interventions should be tested to determine whether they can reduce cancer incidence, morbidity and/or mortality. These hypotheses often will come from basic laboratory, clinical, or epidemiological research which provides evidence for etiological associations or clinical advances for a specific cancer; the basic research itself will not be considered part of cancer control research.

Phase II.
Research on Study Components or Methods Needed to Test the Hypothesis

Methodological research is included here, such as development and testing of questionnaires, studies of compliance, development and testing of screening procedures, pilot tests of the control measures identified in the hypotheses, or testing of methods from other diseases or disciplines on cancer problems.

Phase III.
Case Control Studies and Other Controlled Studies Which Are Not Defined Population Studies

These are research efforts aimed at testing a hypothesis. While the populations may not necessarily be representative of any larger population, the cancer control idea should receive a careful scientific assessment. Certain cohort or cross-sectional studies might be considered here (though technically not case-control), if they do not meet the criteria for a defined population study. Controlled studies of cancer control measures or interventions, which test the efficacy of the measure, would be appropriate here. Phase III studies should incorporate the results of Phase II studies in their design.

Phase IV.
Defined Population Studies

The primary aim of these studies is to allow estimates of the potential impact of the control measures if more broadly applied to a major segment, or the entire population, of the United States. Therefore, in these studies, the denominator as well as the numerator populations must be identified. Thought should be given to how well the defined population represents the larger population to which results may later be generalized. These studies may avoid the selection biases in some case-control studies. Phase III studies generally precede Phase IV studies, and should justify undertaking the Phase IV study.

Phase V.
Demonstration and Implementation Studies

This phase follows careful research in each of the preceeding phases and must be justified on the basis of these earlier studies. It includes research and evaluation efforts related to the demonstration and implementation studies.

As new studies are planned, the background or rationale for each study should identify research results from earlier studies that justify the phase of the proposed study. For example, if a Phase III study is proposed, what research has been done of the Phase I or Phase II types; if a Phase V study is proposed, what research has been done of Phases I-IV types? Note that Phase IV defined population studies precede Phase V demonstration and implementation projects.

(Comments and suggestions about how this classification system may be improved are welcome, including suggestions for modifying or expanding the definitions of the various phases in order to cover the total scope of cancer control research.)

IV. CANCER CONTROL SCIENCE PROGRAM: SCOPE AND CONTENT

The purpose of this program announcement is to encourage the development of Cancer Control Science Programs (CCSP). Grants under this announcement will support a number of CCSPs throughout the United States which together with the Cancer Control Research Units, will be designed to plan and implement cancer control research studies and to serve as a resource for the cancer control research program of the National Cancer Program.

The CCSP is designed to provide support for: a core group of researchers who will perform cancer control research studies; a minimum of three cancer control research projects which can successfully undergo review for scientific merit; developmental funds for pilot projects which are of high scientific merit and have future promise of becoming supported as individual peer reviewed research projects; and other resources, such as data support, which can be justified as necessary to achieve the goals of the CCSP.

V. MECHANISMS OF SUPPORT

The DRCCA, NCI, intends to support these CCSPs as grants for project periods of up to five years. New competing applications will undergo review for scientific merit by an NCI review group and subsequent review by the National Cancer Advisory Board. Renewal of the initial award beyond five years will be contingent upon satisfactory review of a competing renewal application. A maximum of $7.5 million will be available for the combination of the Cancer Control Science Program and the Cancer Control Research Units for the first year of support (FY 1983).

VI. METHOD OF APPLYING

Detailed "Cancer Control Science Program: Guidelines" are available which describe further the scope of cancer control research, the eligibility for application, the letter of intent procedure, and the review procedures and criteria. A letter of intent should be submitted and discussions with Program staff held before a grant application can be submitted. An institution wishing to participate in this effort must submit an application in accordance with the guidelines specified in the CCSP Guidelines.

VII. APPLICATION DATES

	Letter of Intent due Dates	Application Receipt Dates	Initial Review Dates	NCAB Review Dates	Earliest Beginning Dates
First Cycle:	May 15, 1982	Aug. 15, 1982	Sept-April	May 1983	Jul 1,1983
Subsequent cycles:	Sept. 15	Feb. 1	June	Sept. Oct.	Dec. 1
	Jan. 15	June 1	Oct. Nov.	Jan. Feb.	April 1
	May 15	Oct. 1	Feb. March	May	July 1

VIII. INQUIRIES AND CORRESPONDENCE

Carlos E. Caban, Ph.D.
Program Director
Division of Resources, Centers and
Community Activities
National Cancer Institute
Blair Building, Room 716B
8300 Colesville Road
Silver Spring, Maryland 20910

Telephone: (301) 427-8663

ANNOUNCEMENT

MINORITY HYPERTENSION RESEARCH DEVELOPMENT SUMMER PROGRAM

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE
DIVISION OF HEART AND VASCULAR DISEASES

Application Receipt Date: September 15, 1982

The Division of Heart and Vascular Diseases of the National Heart, Lung, and Blood Institute is accepting competing and renewal applications for Institutional National Research Service Awards for research training under the Minority Hypertension Research Development Summer Program.

The Minority Hypertension Research Development Summer Program is intended to (1) encourage the recruitment and development of minority investigators in specialized areas of research, prevention, control and education related to hypertension and (2) stimulate hypertension research, prevention, control and education by offering minority school faculty members and graduate students the opportunity to enhance their research capabilities in these areas.

Training will be offered through HYPERTENSION TRAINING CENTERS which have well-established hypertension research and training programs and are within 100 miles of (a) minority school(s) or provide satisfactory alternative arrangements for communication and exchange. The centers will collaborate with minority schools to work out plans for the identification, selection and development of participating minority school faculty members or graduate students.

Minority schools are those in which a majority or significant proportion of its enrollment is comprised of students of minority ethnic groups-including, but not limited to, Blacks, Spanish-speaking Americans, Native Americans, Pacific Islanders and Asian Americans-and has a demonstrated commitment to the special encouragement of minority faculty, students, and investigators. The Minority School must commit itself to encouraging appropriate faculty members or graduate students to participate in this program, to continue the faculty members or graduate students in status after the summer session, and guarantee at least limited resources for his or her hypertension research and teaching activities.

Participating faculty members or graduate students must be nominated by the Minority School, be accepted by the Training Center, and agree to report annually for six years after training on his or her academic status, publications, grants or contracts and teaching activities related to hypertension.

This program is described in the Catalog of Federal Domestic Assistance No. 13.837, Heart and Vascular Diseases Research. Awards will be made under the authority of the Public Health Service Act, Section 472, 42 USC 289l-1, and administered under PHS grants policy and Federal Regulations 42 CFR Part 66. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

Applications may request funds to provide stipends for the duration of a summer program of $1,115-$1,565 per month for minority school faculty member participants and $420 per month for minority school graduate student participants. In addition, funds may be requested for trainee travel; tuition and fees essential to the training; health insurance coverage for participants during the summer session; and up to $1,250 per faculty member and $750 per graduate student for institutional allowances which includes personnel, supplies, equipment essential to the program and consultant costs when specifically justified. Indirect cost allowances will be limited to 8 percent of the total allowable direct costs or the actual rate, whichever is lower. These budget items are subject to administrative revision.

The present announcement is for a single competition with a September 15, 1982 receipt date for applications. These applications will be reviewed at the February 1983 meeting of the National Heart, Lung, and Blood Advisory Council. The meritorious ones will be awarded beginning May 1, 1983. Applications not received by September 15, 1982, will be returned to the applicant. Guidelines for the development of the application may be obtained by contacting Dr. George A. Hayden at (301) 496-1724.

LETTER OF INTENT

Prospective Training Center applicants should submit a letter of intent not later than May 15, 1982 to:

Dr. George A. Hayden
Research Training and Development Branch
Division of Heart and Vascular Diseases
National Heart, Lung, and Blood Institute
Federal Building, Room 3A-08
Bethesda, Maryland 20205

The Institute requests such letters to obtain an indication of the number and the scope of applications which will require merit review. A letter of intent is not binding and will not enter into the review of any proposal subsequently submitted. The letter should briefly describe the composition of the Hypertension Training Center, participating Minority Institutions, the overall approach, and areas of interest for the Minority Hypertension Research Development Summer Program.

ANNOUNCEMENT

SMALL VESSEL PROSTHESES

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

The National Heart, Lung, and Blood Institute encourages interested investigators to submit research grant applications which will lead to the development and clinical application of small caliber (5 mm or less) vascular grafts. Applications received in response to this Program Announcement will be assigned by the Division of Research Grants to study sections for review according to the NIH process for regular research grant applications. Funding for this activity is in competition with all regular competing grant applications. The purpose of this Program Announcement is to inform the scientific community of the need for additional work in this area. The long-range goal of this program is to develop natural or synthetic graft materials and the clinical protocols for implantation of small caliber vascular prostheses in humans. The development of successful small vessel prostheses may involve contributions from materials science, surface chemistry, rheology, pharmacology, hematology, vascular surgery and veterinary medicine.

The National Heart, Lung, and Blood Institute has a specific interest in supporting research which will lead to an understanding of the basic mechanisms of graft failure and/or lead to potential solutions to problems with current small vessel prostheses. In current surgical practice, autologous vascular tissue is used whenever possible for repair or replacement procedures involving small caliber vessels because these tissues maintain patency better than commercially available prostheses. There is a clinical need for small caliber grafts which will remain patent when used in coronary bypass, in vascular repair in the pediatric patient, in peripheral vascular surgery, and in vascular access for renal dialysis or chemotherapy. Grafts with poor runoff are particularly prone to failure. Intimal proliferation in the graft itself or in the distal vascular bed is a frequent cause of failure. Furthermore, the vascular beds proximal and distal to the graft may become compromised by progression of atherosclerosis, thereby reducing flow and leading to failure. A number of failure mechanisms have been hypothesized but appropriate means to prevent or correct such failures have not been identified.

The recommendations of the Workshop on Vascular Prostheses (NIH Publication No. 82-1215) identified a number of research areas which could lead to development of improved grafts. These areas include better understanding of the role of surface chemistry, physical chemistry and bulk engineering properties of graft materials in success or failure, including the mechanism of failure at the suture line; role of fluid dynamics; understanding of mechanisms which would promote human endothelial cells to populate the graft intima; and development of an appropriate animal model which will accurately predict clinical performance.

This program is described in the Catalog of Federal Domestic Assistance number 13.837, Heart and Vascular Diseases Research. Grants will be awarded under the authority of the Public Health Service Act, Section 301 (42 USC 241) and administered under PHS grant policies and Federal Regulations, most specifically at 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

Applicants submitting responses to this announcement are encouraged to have a clearly focused hypothesis regarding the failure mechanism of currently available materials when used as grafts of this small size in humans. Any one of a number of approaches could be appropriate, including research plans which propose a direct demonstration of the importance of this failure mechanism, or which seek new ways to prevent failure. Some applicants may prefer to test grafts or grafting procedures while others examine relevant discrete components of the problem. As with any research grant application, the choice of a well-controlled experimental design could be an important consideration, since graft failure may be the result of complex interactions.

Potential studies might involve investigation and demonstration of failure mechanisms at low flow using model systems and/or through analysis of retrieved implants, development of new materials with appropriate characterization and validation, identification of pharmacologic regimens to prevent failure, or development and validation of animal models for specified applications; other topic areas may also be appropriate. Research may involve currently available or new materials; studies may be conducted in animals, or in adults or children with due regard for all relevant ethical considerations.

Careful delineation of the methods to be used to characterize the experimental system is encouraged, particularly with regard to physical and chemical properties of graft materials, verification of flow rates, surgical techniques, numbers of animal or data points in a group, and frequency of collection of data points. A clear definition of the experimental end point could be helpful to the reviewers, as well as the criteria to be used to determine whether the hypothesis has been confirmed. Since a proposed hypothesis may already have been discussed within the community or may already be accepted as fact, an explanation of the new information to be gained from the proposed work, its need, and its relative importance may be appropriate.

Support for this research is available through investigator initiated research grants. Application receipt dates are July 1, November 1, and March 1. Applications should be submitted on form PHS 398; these forms are available in the business or grants and contracts office at most academic and research institutions or from the Division of Research Grants, NIH. In order to identify the application as a response to this program announcement, check "yes" on Item 2 of the application face page with the title SMALL VESSEL PROSTHESES. The original and six copies should be submitted to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
Bethesda, Maryland 20205

An additional copy of the application should be mailed to:

Dr. Frances A. Pitlick
Devices and Technology Branch
National Heart, Lung, and Blood Institute
Federal Building, Room 312
7550 Wisconsin Avenue
Bethesda, Maryland 20205

Requests for additional information or questions regarding this program may be directed to Dr. Pitlick at (301) 496-1586.

RESEARCH GRANTS IN NEURAL REGENERATION, NEURAL PLASTICITY AND RELATED DEVELOPMENTAL BIOLOGY

NATIONAL INSTITUTE OF NEUROLOGICAL AND COMMUNICATIVE DISORDERS AND STROKE

Injury to the nervous system entails exceptional physical, financial and emotional hardship on persons directly affected and on their closest associates, as well as on the community at large. The Stroke and Trauma Program (STP) of the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) encourages the submission of applications for research grants in neural regeneration, neural plasticity and in the developmental biology related to these processes. While the ultimate aim is complete restitution of nervous system function in humans, the STP recognizes that basic as well as clinical studies at all levels are required in order to achieve these goals.

Studies related to neural regeneration and plasticity in the brain, spinal cord and peripheral nervous system are, by their nature, complex and require employment of state-of-the-art biochemical, biophysical, physiological, morphological, behavioral, pathological, pharmacological, immunological and other approaches, either individually or in collaborative settings. Investigators should submit carefully designed, well integrated, and adequately documented research applications.

New insights are sought with respect to factors that may inhibit or facilitate optimal healing as evidenced by return of function in the nervous system to pre-injury levels. Areas of research interest in neural regeneration and plasticity include, but are not limited to, the following examples:

- intracellular and extracellular processes concerned with removal of neural tissue debris;
- post-traumatic neural tissue status including glial and vascular responses to injury;
- trophic and growth factors;
- specifying agents and guidance cues;
- hormonal and enzymatic influences;
- intra- and intercellular signalling;
- molecular or ionic fluxes and cellular constituents, cell membranes and the extracellular milieu;
- synthesis and assimilation of proteins, lipids and carbohydrates associated with regeneration;
- cellular and molecular mechanisms of axoplasmic transport;
- membrane incorporation and membrane properties;
- collateral sprouting and neurite extension;
- regional and cellular metabolism (locally and at a distance) prior to and shortly after injury, as well as during reparative stages;

This program is described in the Cataloge of Federal Domestic Assistance, number 13.853, Stroke and Trauma Research. Grants will be awarded under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems agency review.

- involvement of other supportive elements such as connective and vascular tissues;
- the neurotransmitter, neuroreceptor and neurochemical environment in which regenerative activities occur;
- identification of the tissues, cells and substrates critical to the regeneration process;
- re-establishment of neural connectivity;
- the mechanisms responsible for activation and expression of the genetic features regulating the relevant cellular and extracellular elements (since the ability to regenerate neural and other components is species and tissue related);
- neuronal and supportive cell genetic expression in the developmental and regenerative mode of the nervous sytem;
- neural transplants as an approach to the remediation of specific neurologic deficits and the further definition of the nervous system and its effector organs;
- materials science research (e.g., in the development of substrate prosthetic devices to facilitate regrowth of axons in the injured nervous sytem) suggesting additional approaches to understanding the molecular complexities and interactions associated with outgrowing neurites and their substrates;
- latent synapses, remodelled circuitry, and rehabilitative training following injury;
- behavioral, chemical, functional and structural correlates of restored or revised neural circuits.

Applicants are encouraged to develop and use those new and refined methodologies, instrumentation, and surgical procedures which will permit more detailed determination of features involved in neural regeneration. This includes development and use of pertinent in vivo or in vitro models that may serve to demonstrate factors involved in neural regenerative processes.

Investigators should consider submitting well-focused applications addressing one or more compelling questions related to neural regeneration and/or plasticity. Where sufficient baseline data are available, an approach should be entertained that will help test hypotheses that are pivotal to future studies along specific avenues of research. Proposed mechanisms responsible for observations to date would be of obvious interest to other investigators working in the same or related areas. The application must convey the investigators' ability to employ the methodologies described, e.g., listing relevant publications or the inclusion of preliminary data when available. Methodological as well as experimental controls should be described, especially when non-standard or controversial techniques are proposed. Other important elements may include the sequence and timing of proposed studies, potential difficulties and their resolution, quantitation and management of data where appropriate, and adequate justifications of all budgetary requests.

Applications should be prepared on form PHS 398 following instructions contained in the application kit. These kits are available at most institutional business offices or from the Division of Reserch Grants, NIH. The applications will be judged on scientific merit in accord with NIH policy and procedures involving peer review. Initial review will be by an appropriate study section of the DRG. Final review will be by the National Advisory Neurological and Communicative Disorders and Stroke Council. Applications judged more responsive to program interests of other Institutes at the NIH will be assigned accordingly.

Deadline dates for the receipt of new applications are March 1, July 1, and November 1.

The phrase NEURAL REGENERATION AND PLASTICITY should be typed in item 2, of the first (face) page of the application. The original and six copies of the application should be mailed to the following address:

Division of Research Grants
National Institutes of Health
Room 240, Westwood Building
Bethesda, Maryland 20205

One copy of the application is to be sent to the address below. For additional information applicants are encouraged to contact:

Stroke and Trauma Program
National Institute of Neurological and
Communicative Disorders and Stroke
Room 8A13, Federal Building
Bethesda, Maryland 20205

Telephone: (301) 496-4226

ANNOUNCEMENT

EPIDEMIOLOGY OF ORAL DISEASES IN MINORITIES

NATIONAL INSTITUTE OF DENTAL RESEARCH

The National Institute of Dental Research (NIDR) invites applications for support of epidemiological research related to the oral health problems of racial and ethnic minority groups. Research proposed should go beyond descriptions of the nature and extent of the oral health problems experienced by minorities and should offer hypotheses to be tested that would shed light on the relevant factors and conditions that contribute to the problems.

Research proposed may be directed at one or more of the areas noted below and may be confined to a particular minority group. Applicants are encouraged to offer creative proposals which would help improve the understanding of the oral health problems of minorities and provide insight as to how the oral health status of such groups might be improved.

Identified as particularly appropriate for support by the NIDR are epidemiological studies directed toward the identification of the patterns of occurrence of the oral diseases and conditions noted below, and the factors and conditions, including behavioral factors, responsible for, or contributing to these oral health problems:

- Dental Caries, including the prevalence of both coronal and root caries in different age groups;
- Periodontal Diseases, studies using new methodologies for objective measurement of disease activity;
- Congenital Craniofacial Anomalies (including cleft palate), Dentofacial Malrelations, and Acquired Craniofacial Defects;
- Oral Malignancies, Other Oral Soft Tissue Diseases, and Nutritional Deficiencies with Oral Manifestations.

The deadlines for the receipt of research grant applications by the Division of Research Grants are March 1, July 1, and November 1. Review and award of such applications will be through the usual NIH procedures governing research project grants. The award of grants pursuant to this announcement is contingent upon the receipt of responsive proposals of high scientific merit and the availability of appropriated funds.

This program is described in the Catalog of Federal Domestic Assistance Numbers 13.840, 13.841, 13.842, 13.844, and 13.878. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

Applications should be submitted on Form PHS 398, which is available in the business or grants office at most academic or research institutions. If not, application forms may be obtained from:

Office of Grants Inquiries
Division of Research Grants
National Institutes of Health
Room 448, Westwood Building
Bethesda, Maryland 20205

Inquiries regarding this announcement may be directed to one or more of the individuals noted below according to the particular area of concern that the applicant wishes to address:

Dr. John D. Townsley
Caries Research Grants and Contracts Branch
Telephone: (301) 496-7884

Dr. Samuel Kakehashi or
Dr. Paul F. Parakkal
Periodontal Diseases Program Branch
Telephone: (301) 496-7784

Dr. Jerry D. Niswander or
Dr. John D. Suomi
Craniofacial Anomalies Program Branch
Telephone: (301) 496-7807

Dr. Paul D. Frazier or
Dr. David A. Wolff
Soft Tissue Stomatology and Nutrition
Program Branch
Telephone: (301) 496-7807

Dr. Aaron Ganz or
Dr. Patricia S. Bryant
Pain Control and Behavioral Studies
Program Branch
Telephone: (301) 496-7491

The mailing address of the above individuals is:

National Institutes of Dental Research
National Institutes of Health
Westwood Building
Bethesda, Maryland 20205

ANNOUNCEMENT

ENVIRONMENTAL MEDICINE - DEVELOPMENT OF DIAGNOSTIC TECHNOLOGY FOR USE IN POPULATIONS EXPOSED TO HAZARDOUS CHEMICALS, PARTICULARLY FROM WASTE DUMPS

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

The National Institute of Environmental Health Sciences (NIEHS) is the principal Federal agency for biomedical research on the effects of chemical, physical and biological environmental agents on man's health and well being. The Institute supports efforts to identify potentially hazardous environmental agents, including the development, testing, and validation of biological test systems which can be used to measure and predict human toxicity from exposure to environmental factors.

BACKGROUND

Laboratory tests that measure various physiologic and biochemical parameters indicative of normal and abnormal function in many organs and organ systems have been developed and are useful in clinical investigation and research. However, either because these tests have not been so employed, or because specific tests have not yet been developed, few data exist from human studies which support the predictive information obtained from other sources.

For example, while short-term laboratory tests to detect evidence of exposure to mutagens or mutation or other aspects of toxicity are in various stages of development in laboratories throughout the research community, validation of these tests clinically and epidemiologically would allow them to be used in innovative and productive ways to investigate the role of environmental agents in causing disease. The primary usefulness of such tests would be in the detection of subclinical toxicity in advance of the clinical diagnosis of cancer, reproductive, genetic or other abnormalities.

RESEARCH GOALS AND SCOPE

The NIEHS is interested in research applications concerned with the use of laboratory or clinical tests that will aid in the detection and measurement of toxicity to man from chemical exposure at levels which do not produce overt acute symptoms, but which may produce detectable damage years later. Such tests may be of value in assessing adverse health effects due to the exposure of individuals to chemicals. Ideally, the tests would be noninvasive although minimally invasive procedures requiring venipuncture or collection of body fluids may be necessary to measure some known phenomenon associated with biological-chemical interaction such as cytochrome P-450 enzyme induction due to polycyclic hydrocarbon exposure, or change in cholinesterase activity following pesticide exposure.

This program is described in the Catalog of Federal Domestic Assistance No. 13.892, Prediction, Detection and Assessment of Environmentally Caused Diseases and Disorders. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

The goal of this announcement, therefore, is to encourage submission of research applications to evaluate or refine established or newly developed tests with prognostic characteristics in order to assess the effects of exposures that may occur in occupational settings, therapeutic regimes or unexpected episodes of chemical exposure such as might occur with populations exposed to hazardous chemical wastes. Proposed studies may be at the basic biochemistry or cellular pathology level for the purpose of test development within the laboratory setting.

Projects in general would be expected to be of a collaborative nature involving, for example, epidemiologists, clinicians, and laboratory scientists. Projects involving the clinical evaluation of persons who have experienced unique environmental exposures are of particular interest.

Individuals wishing additional information or having questions concerning this program announcement should contact:

Dr. Edward Gardner, Jr.
Program Director
Regular Research Programs Section
Scientific Programs Branch
Extramural Program
NIEHS
P.O. Box 12233
Research Triangle Park, N.C. 27709

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NIH GUIDE for GRANTS and CONTRACTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Vol. 11, No. 5, April 23, 1982

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HAVE YOU MOVED?

If your present address differs from that shown on the address label, please send your new address to: Grants and Contract Guide Distribution Center, National Institutes of Health, Room B3BN10, Building 31, Bethesda, Maryland 20205, and attach your address label to your letter. Prompt notice of your change of address will prevent your name from being removed from our mailing list.

The GUIDE is published at irregular intervals to announce scientific initiatives and to provide policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in grants and contracts activities administered by the National Institutes of Health.

Two types of supplements are published by the respective awarding units. Those printed on yellow paper concern contracts: solicitations of sources and announcement of availability of requests for proposals. Those printed on blue paper concern invitations for grant applications in well-defined scientific areas to accomplish specific program purposes.

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NOTICE TO NRSA TRAINING PROGRAM DIRECTORS

The Omnibus Reconciliation Act (P.L. 97-35) modified the provision for National Health Service Corps (NHSC) Scholarship recipients explicitly to indicate that they could receive payback credit through either the institutional or individual component of the National Research Service Award (NRSA) program. Prior to the signing of the act on August 13, 1981, only NHSC recipients who received individual NRSA awards were permitted to receive credit towards the NHSC service obligation for any payback obligation performed as a requirement of the NRSA program. This option is being extended to NHSC recipients who wish to participate as trainees under the NRSA Institutional Grant Program.

You may be contacted by one or more of these individuals seeking an appointment as a postdoctoral trainee on your training program. Qualified candidates from the NHSC should be considered along with other applicants when appointments are made. Selection of NHSC applicants would help further the intent of Congress as expressed in the NRSA legislation that special consideration be given to physicians who will spend two years in research.

NOTICE

ERRATA

An Announcement in the March 26, 1982 Guide for Grants and Contracts (Vol. 11, No. 4) entitled "Special Emphasis Research Career Award: Diabetes Mellitus-Obstetrical, Perinatal, and Pediatric Aspects, National Institute of Child Health and Human Development" has a line missing from the text at the top of page 7. The correct wording should be as follows:

> "oriented around the initiation of a specific research program of the applicant's own"

NOTICE

CHANGES IN EXPENDITURES REPORTING FORMS FOR NIH AND ADAMHA GRANTEES

In April 1979, a notice in the "NIH Guide for Grants and Contracts (Vol. 8, No. 5)" apprised grantees of the schedule to be followed by NIH and ADAMHA for conversion from categorical expenditures reporting to non-categorical reporting. This change was the result of DHHS' implementation of OMB Circular A-110. Specifically, the announcement said that a non-categorical Financial Status Report "will be used to report on all budget periods whose start dates were October 1, 1978, and thereafter." However, as an interim measure, the NIH was later authorized to continue using form HEW-489, which was familiar to NIH staff and its grantees, but with revised instructions indicating that the reporting of detailed categorical expenditures was no longer mandatory. ADAMHA also followed this interim approach.

Recently the Office of Management and Budget advised the NIH to adopt form SF-269, "Financial Status Report" (see reduced format attached) for use by all grantees in reporting the status of funds for all nonconstruction grants. This action is in keeping with the intent of OMB Circulars A-102 and A-110 to standardize certain Federal reporting requirements. Therefore, it is now necessary for NIH and ADAMHA grantees to start using the SF-269 Federal-wide reporting form as promptly as possible. Since it will take a little time before the forms are stocked in bulk and the offices responsible for distribution can begin sending out copies routinely, those grantees who must submit reports may continue to use the HEW-489 forms which they have on hand during the transition period.

2A

FINANCIAL STATUS REPORT

(Follow instructions on the back)

1. FEDERAL AGENCY AND ORGANIZATIONAL ELEMENT TO WHICH REPORT IS SUBMITTED

2. FEDERAL GRANT OR OTHER IDENTIFYING NUMBER

OMB Approved No 80-RO180

PAGE OF PAGES

3. RECIPIENT ORGANIZATION *(Name and complete address, including ZIP code)*

4. EMPLOYER IDENTIFICATION NUMBER

5. RECIPIENT ACCOUNT NUMBER OR IDENTIFYING NUMBER

6. FINAL REPORT ☐ YES ☐ NO

7. BASIS ☐ CASH ☐ ACCRUAL

8. PROJECT/GRANT PERIOD *(See instructions)*
FROM *(Month, day, year)*
TO *(Month, day, year)*

9. PERIOD COVERED BY THIS REPORT
FROM *(Month, day, year)*
TO *(Month, day, year)*

10.	STATUS OF FUNDS						
PROGRAMS/FUNCTIONS/ACTIVITIES ▶	*(a)*	*(b)*	*(c)*	*(d)*	*(e)*	*(f)*	TOTAL *(g)*
a. Net outlays previously reported	$	$	$	$	$	$	$
b. Total outlays this report period							
c. *Less:* Program income credits							
d. Net outlays this report period *(Line b minus line c)*							
e. Net outlays to date *(Line a plus line d)*							
f. *Less:* Non-Federal share of outlays							
g. Total Federal share of outlays *(Line e minus line f)*							
h. Total unliquidated obligations							
i. *Less:* Non-Federal share of unliquidated obligations shown on line h							
j. Federal share of unliquidated obligations							
k. Total Federal share of outlays and unliquidated obligations							
l. Total cumulative amount of Federal funds authorized							
m. Unobligated balance of Federal funds							

11. INDIRECT EXPENSE
a. TYPE OF RATE *(Place "X" in appropriate box)* ☐ PROVISIONAL ☐ PREDETERMINED ☐ FINAL ☐ FIXED

b. RATE	c. BASE	d. TOTAL AMOUNT	e. FEDERAL SHARE

12. REMARKS: *Attach any explanations deemed necessary or information required by Federal sponsoring agency in compliance with governing legislation.*

13. CERTIFICATION
I certify to the best of my knowledge and belief that this report is correct and complete and that all outlays and unliquidated obligations are for the purposes set forth in the award documents.

SIGNATURE OF AUTHORIZED CERTIFYING OFFICIAL

DATE REPORT SUBMITTED

TYPED OR PRINTED NAME AND TITLE

TELEPHONE *(Area code, number and extension)*

269-102

STANDARD FORM 269 (7-76)
Prescribed by Office of Management and Budget
Cir. No. A-110

INSTRUCTIONS

Please type or print legibly. Items 1, 2, 3, 6, 7, 9, 10d, 10e, 10g, 10i, 10l, 11a, and 12 are self-explanatory, specific instructions for other items are as follows:

Item	*Entry*
4	Enter the employer identification number assigned by the U.S. Internal Revenue Service or FICE (institution) code, if required by the Federal sponsoring agency
5	This space is reserved for an account number or other identifying numbers that may be assigned by the recipient.
8	Enter the month, day, and year of the beginning and ending of this project period. For formula grants that are not awarded on a project basis, show the grant period.
10	The purpose of vertical columns (a) through (f) is to provide financial data for each program, function, and activity in the budget as approved by the Federal sponsoring agency. If additional columns are needed, use as many additional forms as needed and indicate page number in space provided in upper right; however, the totals of all programs, functions or activities should be shown in column (g) of the first page. For agreements pertaining to several Catalog of Federal Domestic Assistance programs that do not require a further functional or activity classification breakdown, enter under columns (a) through (f) the title of the program. For grants or other assistance agreements containing multiple programs where one or more programs require a further breakdown by function or activity, use a separate form for each program showing the applicable functions or activities in the separate columns. For grants or other assistance agreements containing several functions or activities which are funded from several programs, prepare a separate form for each activity or function when requested by the Federal sponsoring agency.
10a	Enter the net outlay. This amount should be the same as the amount reported in Line 10e of the last report. If there has been an adjustment to the amount shown previously, please attach explanation. Show zero if this is the initial report.
10b	Enter the total gross program outlays (less rebates, refunds, and other discounts) for this report period, including disbursements of cash realized as program income. For reports that are prepared on a cash basis, outlays are the sum of actual cash disbursements for goods and services, the amount of indirect expense charged, the value of in-kind contributions applied, and the amount of cash advances and payments made to contractors and subgrantees. For reports prepared on an accrued expenditure basis, outlays are the sum of actual cash disbursements, the amount of indirect expense incurred, the value of in-kind contributions applied, and the net increase (or decrease) in the amounts owed by the recipient for goods and other property received and for services performed by employees, contractors, subgrantees, and other payees.
10c	Enter the amount of all program income realized in this period that is required by the terms and conditions of the Federal award to be deducted from total project costs. For reports prepared on a cash basis, enter the amount of cash income received during the reporting period. For reports prepared on an accrual basis, enter the amount of income earned since the beginning of the reporting period. When the terms or conditions allow program income to be added to the total award, explain in remarks, the source, amount and disposition of the income.
10f	Enter amount pertaining to the non-Federal share of program outlays included in the amount on line e.
10h	Enter total amount of unliquidated obligations for this project or program, including unliquidated obligations to subgrantees and contractors. Unliquidated obligations are: Cash basis—obligations incurred but not paid; Accrued expenditure basis—obligations incurred but for which an outlay has not been recorded. Do not include any amounts that have been included on lines a through g. On the final report, line h should have a zero balance.
10j	Enter the Federal share of unliquidated obligations shown on line h. The amount shown on this line should be the difference between the amounts on lines h and i.
10k	Enter the sum of the amounts shown on lines g and j. If the report is final the report should not contain any unliquidated obligations.
10m	Enter the unobligated balance of Federal funds. This amount should be the difference between lines k and l.
11b	Enter rate in effect during the reporting period.
11c	Enter amount of the base to which the rate was applied.
11d	Enter total amount of indirect cost charged during the report period.
11e	Enter amount of the Federal share charged during the report period. If more than one rate was applied during the project period, include a separate schedule showing bases against which the indirect cost rates were applied, the respective indirect rates the month, day, and year the indirect rates were in effect, amounts of indirect expense charged to the project, and the Federal share of indirect expense charged to the project to date.

ELIGIBILITY OF FOR-PROFIT ORGANIZATIONS TO APPLY FOR NIH GRANTS AND COOPERATIVE AGREEMENTS

NOTICE

Effective January 4, 1982, for-profit organizations became eligible to apply for assistance awards (research grants and cooperative agreements) under most sections of the Public Health Service Act.

The application, scientific merit review, and award processes are the same as those applicable to nonprofit organizations. All information contained in applications will be kept confidential and will be made available only to NIH staff and to the reviewers who provide an evaluation of the proposed project. Applications for research projects are to be submitted on application form PHS-398 which may be obtained from:

Office of Grants Inquiries
Division of Research Grants
National Institutes of Health
Westwood Building, Room 449
5333 Westbard Avenue
Bethesda, Maryland 20205

Annual application receipt dates are on or before: July 1, November 1, and March 1. Applications are sent to the Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20205.

For-profit organizations will be subject to the same administrative requirements applicable to nonprofit organizations with a few exceptions:

1. Cost principles for Contracts with Commercial Organizations set forth in 41 CFR Subpart 1-15.2 will be used.
2. Title to equipment and supplies acquired under the financial assistance award shall vest upon acquisition in the Federal government. Subsequent disposition will be determined by the PHS awarding office.
3. Cost sharing requirements will be met through separate agreements negotiated for each project.
4. Development, reporting, and disposition of patents and inventions, will be governed by the terms of the Patent and Trademark Law Amendments (P.L. 96-517), which was effective July 1, 1981.
5. Program income, as defined in 45 CFR 74.42, earned during the period of PHS grant support, no matter what the purpose, may not be used for costs which are in addition to the allowable costs of the project.

Research scientists from for-profit organizations are encouraged to request a copy of NIH Extramural Programs, a compendium of the scientific programs of the NIH's Bureaus, Institutes, and Divisions. Address such requests to the Office of Grants Inquiries, Division of Research Grants, (address above).

NOTICE

REQUEST FOR NOMINATIONS OF INDIVIDUALS FROM FOR-PROFIT ORGANIZATIONS TO SERVE AS MEMBERS OF NIH SCIENTIFIC REVIEW GROUPS

The National Institutes of Health (NIH) invites nominations of individuals representing for-profit organizations for membership on its scientific peer review groups. These groups provide the technical and scientific merit review of grant and cooperative agreement applications and contract proposals. Scientists serving on these groups advise the NIH on the selection of the most meritorious projects to implement biomedical research programs of the highest quality. Although a number of scientists from commercial organizations now serve on these advisory bodies, because of the recently declared eligibility of for-profit organizations to apply for research grants, NIH has a special interest in adding greater representation from this scientific sector than now exists.

All nominations will be carefully considered; NIH reserves the right to make final selections.

Responsibilities

Each review group is composed of primarily non-Federal scientists selected for their competence in the particular scientific area for which that group has review responsibilities. Review groups usually meet three times yearly; each meeting generally requires several days of intensive review of research proposals. Specific applications are assigned in advance of the meeting to each member who prepares written detailed critiques prior to the meeting and leads discussion at the meeting. Members generally serve terms not to exceed four years.

Criteria for Membership

The primary requirement for serving on a scientific review group is competence as an independent investigator in a basic scientific or clinical discipline or research specialty. Assessment of such competence is based on the quality of research accomplished, publications in refereed scientific journals, and other significant scientific activities, achievements, and honors. Usually a doctoral degree or its equivalent is required. Service also requires mature judgment, balanced perspective, objectivity, ability to work effectively in a group context, commitment to complete work assignments, and assurance that the confidentiality of applications will be protected.

How to Respond to Request

Any person may nominate one or more highly qualified candidates for consideration. Self-nominations are acceptable. Nominations should be made promptly for immediate consideration, and at any time thereafter for future attention. Each nomination should be clearly identified as representing the for-profit sector.

For each nomination:

1. Provide full name of nominee, title, complete mailing address (including organizational affiliation), and telephone number.
2. In not more than two or three lines, provide in key words information concerning the nominee's scientific areas of experience, interest, and expertise.
3. Name, address, telephone number, and signature of nominator.

The nominator may be contacted for more detailed information. Nominees should be informed prior to being nominated. They will be sent a packet requesting relevant information upon receipt of nomination.

Send information to:

NIH Consultant File Project
Suite 212
6400 Goldsboro Road
Bethesda, Maryland 20817

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA NIH-NIAID 82-7

ASTHMA AND ALLERGIC DISEASE CENTERS

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Application Receipt Date: October 15, 1982

I. BACKGROUND

The National Institute of Allergy and Infectious Diseases (NIAID) invites applications for grants to be initiated during FY 1983 for participation in the ongoing Asthma and Allergic Disease Centers (AADC) program.

The Allergy and Clinical Immunology Branch of the Immunology, Allergic, and Immunologic Diseases program of NIAID sponsors fundamental and clinical research grants and contracts and the procurement and application of research resource and reference reagents concerned with asthma, allergic and immunologic diseases and with relevant mechanisms of hypersensitivity and inflammation. This request for applications is intended to encourage the development of proposals from clinical investigative groups meeting the criteria and requirements for an AADC and to coordinate the submission of new and renewal applications providing equitable opportunity for both to compete for funds currently available for this programmatic activity.

Since its inception in 1971, the AADC program has progressively expanded with the gradual addition of new Centers on an open application basis. In accordance with established policy announced in the NIH Guide for Grants and Contracts, Vol. 7, No. 8, p.1, June 9, 1978, proposals for AADCs are received only periodically and at designated times. Applications for both renewal of existing AADCs and creation of new Center programs will be expected to compete for funds available through the periodically announced awards.

The AADC program currently consists of 17 centers. During FY 1983, five Centers are scheduled to terminate and may compete for renewal.

NIAID's fundamental objective in continuing the AADC program remains unchanged: acceleration of the application of emerging knowledge on the immune system and from relevant biomedical sciences to clinical investigations concerned with asthma, allergic diseases, and hypersensitivity disorders. Especially sought as the requisite factors within a participating institution are quality research in (a) basic sciences(s), (b) clinical investigation supported by adequate clinical facilities, staff expertise in diagnosis and management of asthmatic and allergic patients, and

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This program is described in the Catalog of Federal Domestic Assistance No. 13.855, Immunology, Allergic and Immunologic Diseases Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR 74). This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

(c) access to (an) appropriate patient population(s) within a suitable academic/investigative setting designed to favor multidisciplinary interaction.

II. RESEARCH GOALS AND SCOPE

A. There should be indication by the sponsoring university or medical institution of willingness and preparedness to commit resources to ensure development, operation, support, and function of the proposed Center in devoting its efforts to an identified study on asthma and/or allergic disease as a fundamental prerequisite.

B. The applicant's achievements in basic science research should have reached that stage of development where experimental leads are sufficiently encouraging to warrant transition from promising laboratory findings to corresponding investigations at the clinical level with the ultimate goal of developing new and improved methods for diagnosis, prevention, and treatment of asthma and/or the other allergic diseases.

C. A prospective Center should be in a position to present evidence of experience orientation, laboratory and clinical facilities, scientific and professional staff, support personnel and the expertise to design proposals, execute protocols representing a multifaceted long-term approach, and bring diverse institutional strengths to bear upon the study of major problems in asthma, other allergic diseases and/or pathophysiologic mechanisms underlying these disorders.

D. Suitable subjects for study within the provision of this program may include those relevant to:

1. Asthma and its multifactoral aspects;
2. Atopic diseases (e.g., allergic rhinitis, urticaria, atopic dermatitis);
3. Identification, isolation, and characterization of etiologic agents of allergy (e.g., drugs, chemicals, foods, airborne allergens);
4. Pathologic expressions, pathophysiologic mechanisms, and genetic factors of allergic disease and allergic inflammation;
5. Immune mechanisms and agents of immediate hypersensitivity and of related hypersensitivity manifestations of antigen-antibody reactions of cell mediated immunity (e.g., hypersensitivity pneumonitis, allergic dermatitis, vasculitis, allergic gastroenteritis, drug reactions) and the development of corresponding improved diagnostic materials and methods;
6. Immunopharmacology, immunotherapy, and the development of specific pharmacologic agents designed for prevention and treatment of asthma and the other allergic diseases.

E. Study of animal models will be considered acceptable as a partial segment or adjunct to a Center's program only if this line of research is applicable to the character of the primary investigation of asthma or the human allergic disease central to the proposal.

F. Designation of a Center Director should be based upon accomplishment and experience as a senior scientist and ability to assume both leadership of the investigative group and responsibility for scientific, professional, and administrative functions.

G. More than one delineated avenue of research may be pursued within a Center with provision for unified operation and coordination of component projects and collaborative investigators.

H. A Center should not rely upon its ability to conduct research activity solely within the confines of a single discipline, but rather should have established the associations to involve participation by workers in the pertinent biomedical fields and medical specialties allied to asthma, allergy, and clinical immunology (e.g., dermatology, rheumatology, infectious diseases, pulmonary medicine, hematology, otorhinolaryngology, when a high degree of relevance to immunology exists).

I. The Center Director will be expected to communicate freely with the NIAID and other designated Centers for effective exchange of new information, to interact with scientists working in other Centers on related investigative problems, and to present progress reports and share experimental data with other Centers through exchanges and attendance at NIAID sponsored meetings of study groups and AADC workshops.

III. MECHANISM OF SUPPORT

In Fiscal Year 1983, the NIAID plans to fund at least five new or competing renewal Asthma and Allergic Disease Center applications. Each grant will have a duration of not more than five years. Funding beyond the first year of the grant will be contingent upon satisfactory progress during the preceding year and availability of funds.

The receipt date for applications will be October 15, 1982. They will undergo initial review in February-March 1983, and subsequent review by the National Advisory Allergy and Infectious Diseases Council in May 1983. September 1, 1983 will be the earliest starting date for successful applicants.

Grant funds may be utilized to support the research activities of scientific and professional personnel, administration, consultation services, central support services, equipment, supplies, travel, and publication costs. Support for research-related costs of patient involvement and medical care may be authorized. Since the program cannot provide funds for new construction, adequate physical facilities must be available for the primary needs of the Center. However, moderate alterations or renovations to enhance clinical facilities may be allowed if they are necessary to meet objectives of the Center's program.

Only those institutions that can demonstrate expertise in both basic and clinical areas and can direct their resources toward a multifaceted attack on asthma or the other allergic diseases can be supported under the provisions of the AADC program.

IV. REVIEW PROCEDURES AND CRITERIA

A. For preliminary screening by NIAID staff, a "letter of intent" should first be prepared by the prospective Center Director. Letters of intent should cover the following points:

1. A brief description of the intended project.
2. A description of available laboratory facilities.
3. A brief description of ongoing basic immunologic and clinical research relating to asthma, allergy, or hypersensitivity with special reference to any studies of the immediate type.
4. A brief description of, or reference to, published research work by the investigators on asthma, allergy, or hypersensitivity especially pointing out those that may relate to the immediate type and identification of existing projects and sources of support.
5. A description of all clinic facilities available for use by the proposed Center.
6. Specific information on the institution's present patient load and projections for patient involvement in clinical investigation.
7. The academic positions and major research interests of the Center Director and his professional staff who will be involved in the work of the Asthma and Allergic Disease Center.
8. Collaborative possibilities with other area laboratories and investigators and delineation of the roles and manner of anticipated participation and interaction of the principal investigators, consultants, and collaborators.

B. Letters of intent are due no later than July 15, 1982, and upon receipt will be screened by NIAID staff to determine the eligibility and suitability of the projected proposals for the AADC program. Inquiries and letters should be sent to:

Dr. Robert A. Goldstein
Chief, Allergy and Clinical Immunology Branch
Immunology, Allergic and Immunologic
Diseases Program
National Institute of Allergy and
Infectious Diseases
National Institutes of Health
Westwood Building Room 755
Bethesda, Maryland 20205

Telephone: (301) 496-7104

V. CONSEQUENCES OF LACK OF RESPONSIVENESS TO THE RFA OR LATE SUBMISSION

Based upon the letter of intent, potential applicants will be promptly advised whether or not their proposal is found to be within the research goals and scope of the program as defined in this RFA. Applicants will then have an opportunity to correct deficiencies or weaknesses and to restructure their submissions accordingly. Formal applications that are not responsive to the RFA or are not received by October 15, 1982, will not be accepted for review and will be returned to the applicant.

VI. METHOD OF APPLYING

Before preparing an application, the prospective applicant should request a copy of the NIAID Information Brochure on Program Projects from:

Dr. Nirmal Das
Executive Secretary
Allergy, Immunology and Transplantation
Research Committee
National Institute of Allergy and
Infectious Diseases
National Institutes of Health
Westwood Building Room 706
Bethesda, Maryland 20205

Telephone: (301) 496-7966

Use the standard research grant application form PHS 398 (Rev. 5/80). In addition to following accompanying format instructions for the development of a Center application, include expanded material listed above under the eight points for the "letter of intent." For purposes of identification and processing, the words "ASTHMA AND ALLERGIC DISEASE CENTER" should be typed in item 2 on the face page of the application and a brief covering letter should be attached indicating submission is in response to this NIAID announcement.

Application kits may be obtained from the institution's application control office. If not available there, they may be obtained from:

Office of Grant Inquiries
Division of Research Grants
National Institutes of Health
Westwood Building Room 448
Bethesda, Maryland 20205

Forward the complete application to:

Division of Research Grants
National Institutes of Health
Westwood Building Room 240
Bethesda, Maryland 20205

Please forward a copy (not the original) of the cover letter and the application face page to Dr. Robert A. Goldstein in order to alert NIAID to the submission of the proposal, and to:

Chief, Program and Project Review Branch
National Institute of Allergy and
Infectious Diseases
National Institutes of Health
Westwood Building Room 703
Bethesda, Maryland 20205

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA NIH-NIAID 82-8

CENTERS FOR INTERDISCIPLINARY RESEARCH ON IMMUNOLOGIC DISEASES

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Application Receipt Date: October 1, 1982

BACKGROUND

The National Institute of Allergy and Infectious Diseases (NIAID) invites applications for grants to be initiated during Fiscal Year 1983 for participation in the ongoing Program of Centers for Interdisciplinary Research on Immunologic Diseases (CIRID).

The Allergy and Clinical Immunology Branch of the Immunology, Allergic, and Immunologic Diseases program of NIAID sponsors fundamental and clinical research grants and contracts and the procurement and application of research resource and reference reagents concerned with asthma, allergic and immunologic diseases and with relevant mechanisms of hypersensitivity and inflammation. This request for applications is intended to encourage the development of proposals from clinical investigative groups meeting the criteria and requirements for a CIRID and to coordinate the submission of new and renewable applications providing equitable opportunity for both to compete for funds currently available for this programmatic activity. Current recipients of Asthma and Allergic Disease Center (AADC) or Program Projects in Mechanisms of Immunologic Diseases Awards are encouraged to apply for a CIRID grant. In the event that such an application is successful, it is NIAID's intention to support only one instrument.

Since its inception in 1978, the CIRID program, which currently consists of four Centers, has progressively matured. Applications for both renewal of existing CIRIDs and creation of new Center programs will be expected to compete for funds available through the periodically announced awards. During FY 1983, four Centers are scheduled to terminate and may compete for renewal.

NIAID's fundamental objective in continuing the CIRID program remains unchanged: acceleration of the application of emerging knowledge on the immune system and from relevant biomedical sciences to clinical investigations concerned with asthma, allergic diseases, hypersensitivity disorders, and immunologically mediated disorders. Especially sought as the requisite factors within a participating institution are quality research in (a) basic science(s), (b) clinical investigation supported by adequate clinical facilities, staff expertise in diagnosis and management of patients with asthma, allergies and other immunologic diseases, and (c) access to (an) appropriate patient population(s) within a suitable academic/investigative setting designed to favor multidisciplinary interaction.

This program is described in the Catalog of Federal Domestic Assistance No. 13.855, Immunology, Allergic and Immunologic Diseases Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

RESEARCH GOALS AND SCOPE

1. There should be indication by the sponsoring university or medical institution of willingness and preparedness to commit resources to ensure development, operation, support, and function of the proposed Center.

2. The applicant institution's achievements in basic science research should have reached that stage of development where experimental leads are sufficiently encouraging to warrant transition from promising laboratory findings to corresponding investigations at the clinical level with the ultimate goal of developing new and improved methods for diagnosis, prevention, and treatment of allergic and immunologic disorders.

3. Centers should be based at universities or at university-affiliated medical facilities. Eligible institutions which already have NIAID supported AADC's or Program Projects are eligible to apply for conversion of ongoing programs to a CIRID.

4. Programs should be signed to favor integration and coordination of intra-institutional research projects concerned with immunologic disease and those in basic biomedical sciences, e.g., immunobiology, immunochemistry, microbiology, virology, genetics, biochemistry, pharmacology, general physiology, and pathology. Programs should also draw upon clinical specialities, e.g., allergy, dermatology, pulmonary medicine, hematology, nephrology, rheumatology, infectious diseases, and otorhinolaryngology.

5. Grants in support of the interdisciplinary research program can be given for periods of up to five years; evaluation of the Centers to ascertain productivity and accomplishments may be undertaken after completion of the third year to aid the NIAID in determining possible future directions for the program.

6. Study of a spectrum of allergic diseases, including asthma, should be recognized as one necessary component of a Center's program in immunologic diseases. Applicant institutions that do not now have ongoing programs in asthma and allergic disease will be expected to describe definitive plans for developing capabilities in these areas during the period of the grant. Applications from institutions whose programs are primarily oriented to asthma and allergic diseases should similarly describe institutional plans for interdisciplinary expansion to include pertinent basic science components and investigations in other immunologic disease areas.

7. Suitable subjects for study within the provision of this program may include those relevant to:

   a. Immunologic disorders;

   b. Asthma and its multifactoral aspect and atopic diseases (e.g., allergic rhinitis, urticaria);

   c. Identification, isolation, and characterization of etiologic agents of allergy (e.g., drugs, chemicals, foods, airborne allergens);

   d. Pathologic expressions, pathophysiologic mechanisms, and genetic factors of allergic disease and allergic inflammation.

8. In addition to developing broad interdisciplinary research programs in immunology, the Centers will be expected to carry out other educational or community activities. Within the research framework the applicant should include as many of the following special projects as the applicant can develop and support:

    a. Recruitment and training of clinical investigators in allergy and clinical immunology.

    b. Development of demonstration programs designed to yield new information on the feasibility of diagnostic methods and treatment.

    c. Assessment of the regional socioeconomic impact of immunologic and allergic diseases through interaction with practicing physicians and epidemiologists in the area.

    d. Evaluation of new treatment modalities and development of methods studying efficacy.

    e. Clinical translation and application of promising investigative findings.

    f. Involvement in the continuing medical education of practicing physicians, and in lay community outreach in the region served.

9. Designation of a Center Director should be based upon accomplishment and expeience as a senior scientist and ability to assume both leadership of the investigative group and responsibility for scientific, professional, and administrative functions.

10. More than one delineated avenue of research may be pursued within a Center with provisions for unified operation and coordination of component projects and collaborative investigators.

11. A Center should not rely upon its ability to conduct research activity solely within the confines of a single discipline, but rather should have established the associations to involve participation by workers in the pertinent biomedical fields and medical specialties allied to asthma, allergy, and clinical immunology (e./g., immunobiology, biochemistry, microbiology, biostatistics, bioinstrumentation and computer science, and the clinical subspecialities, e.g., dermatology, rheumatology, infectious diseases, pulmonary medicine, hematology, otorhinolaryngology, when a high degree of relevance to immunology exists).

12. The Center Director will be expected to communicate freely with the NIAID and other designated Centers for effective exchange of new information, to interact with scientist working in other Centers on related investigative problems, and to present progress reports and share experimental data with other Centers through exchanges and attendance at NIAID sponsored meetings of study groups and AADC-CIRID workshops.

13. Because NIAID intends this program to be as broadly based as possible, attention will be given to geographical dispersion.

MECHANISMS OF SUPPORT

In Fiscal Year 1983, the NIAID plans to fund at least four new or competing renewal CIRID applications. Each Center grant will have a duration of not more than five years. Funding beyond the first year of the grant will be contingent upon satisfactory progress during the preceding year and availability of funds.

The receipt date for applications will be October 15, 1982. They will undergo initial review in February-March 1983, and subsequent review by the National Advisory Allergy and Infectious Diseases Council in May 1983. September 1, 1983 will be the earliest starting date for successful applicants.

Grant funds may be utilized to support the research activities of scientific and professional personnel, administration, consultation services, central support services, equipment, supplies, travel, and publiction costs. Support for research-related costs of patient involvement and medical care may be authorized. Since the program cannot provide funds for new construction, adequate physical facilities must be available for the primary needs of the Center. However, moderate modifications or renovations to enhance clinical facilities may be allowed if they are necessary to meet objectives of the Center's program. Only those institutions that can demonstrate expertise in both basic and clinical areas and can direct their resources toward a multifaceted attack on human immunologic diseases can be supported under the provisions of the CIRID program.

REVIEW PROCEDURES AND CRITERIA

For preliminary screening by NIAID staff, a "letter of intent" should first be prepared by the prospective Center Director.

Letters of intent should cover the following points:

1. A brief description of the intended project.

2. A brief description of available laboratory facilities.

3. A brief description of ongoing basic research and clinical investigations, including reference to published work authored by staff that are relevant to asthma, allergy and immunologic diseases.

4. A brief description of, or reference to, published research work by the investigators on asthma, allergy, or hypersensitivities and identification of existing project and sources of support.

5. A description of all clinical facilities available and plans for their utilization.

6. Specific information on the institution's present patient load and projections for patient involvement in clinical investigations.

7. The academic positions and major research interest of the Center Director and staff who will be involved in the work of the Center.

8. Plans for collaboration with other laboratories and investigators and delineation of the roles and manner of anticipated participation of the principal investigators, consultants, and collaborators and collaborators.

Letters of intent are due no later than July 15, 1982, and upon receipt will be screened by NIAID staff to determine the eligibility and suitability of the projected proposals for the CIRID program.

Inquiries should be sent to:

Dr. Robert A. Goldstein
Chief, Allergy and Clinical Immunology Branch
Immunology, Allergic and Immunologic
Diseases Program
National Institute of Allergy and
Infectious Diseases
National Institutes of Health
Westwood Building Room 755
Bethesda, Maryland 20205

Telephone: (301) 496-7104

CONSEQUENCES OF LACK OF RESPONSIVENESS TO THE RFA OR LATE SUBMISSION

Based upon the letter of intent, potential applicants will be promptly advised whether or not their proposal is found to be within the research goals and scope of the program as defined in this RFA. Applicants will then have an opportunity to correct deficiencies or weaknesses and to restructure their submissions accordingly. Formal applications that are not responsive to the RFA or are not received by October 15, 1982, will not be accepted for review and will be returned to the applicant.

METHOD OF APPLYING

Before preparing an application, the prospective applicant should request a copy of the NIAID Information Brochure on Program Projects from:

Dr. Nirmal Das
Executive Secretary
Allergy, Immunology and Transplantation
Research Committee
National Institute of Allergy and
Infectious Diseases
National Institutes of Health
Westwood Building, Room 706
Bethesda, Maryland 20205

Telephone: (301) 496-7966

In order to assure adequate review it is important to follow instructions in the Information Brochure, which contains details on the format and requirements for multidisciplinary grant applications.

Use the standard research grant application form PHS 398 (Rev. 5/80). In addition to following accompanying format instructions for the development of a Center application, include expanded material listed above under the eight points for the "letter of intent."

For purposes of identification and processing, the words "CENTERS FOR INTERDISCIPLINARY RESEARCH ON IMMUNOLOGIC DISEASES" should be typed in item 2 on the face page of the application and a brief covering letter should be attached indicating submission is in response to this NIAID announcement.

Application kits may be obtained from the institution's application control office. If not available there, they may be obtained from:

Office of Grants Inquiries
Division of Research Grants
National Institutes of Health
Westwood Building Room 448
Bethesda, Maryland 20205

Forward the complete application to:

Division of Research Grants
National Institutes of Health
Westwood Building Room 240
Bethesda, Maryland 20205

Please forward a copy (not the original) of the cover letter and the application face page to: (1) Dr. Robert A. Goldstein in order to alert NIAID to the submission of the proposal, and to:

Chief, Program and Project Review Branch
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Westwood Building Room 703
Bethesda, Maryland 20205

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA NIH-NHLBI-82G-J

DEMONSTRATION AND EDUCATION RESEARCH IN HEART, BLOOD VESSEL, LUNG, AND BLOOD DISEASES AND BLOOD RESOURCES

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Application Receipt Date: October 15, 1982

I. PURPOSE

The objective of this Request for Applications (RFA) is to invite grant applications for demonstration or education research in heart, blood vessel, lung, and blood diseases and blood resources. These research projects must be directed toward some significant aspect of heart, blood vessel, lung, or blood diseases and blood resources. The population in which the research would be conducted should be well defined and include health-care professionals, defined groups within a community, or the general population. Staffing for the research should include relevant expertise of professionals in disciplines as needed, including medical disciplines, health education, epidemiology, biostatistics, and behavioral and social science. To be responsive to this announcement, the applicant institution must have basic and clinical research activities related to the general areas of the proposed demonstration or education research.

II. ELIGIBILITY

To be eligible for competition under this RFA, applicants who propose demonstration or education research projects must also concisely

- describe the institution's ongoing basic and clinical research related to the general area of the proposed demonstration or education project;
- explain the actual or potential value these ongoing basic and clinical research programs have or would have for the proposed demonstration or education research; and
- present evidence that cooperation with all relevant groups has been obtained.

III. BACKGROUND

This Request for Applications (RFA) represents another step toward fulfilling the congressional intent of Public Law 92-423 that the National Heart, Lung, and Blood Institute (NHLBI) establish centers ". . . for basic or clinical research into, trainining in, and demonstration of, advanced diagnostic, prevention, and treatment methods for heart, blood vessel, lung, or blood diseases." The goal of this authorization was to stimulate rapid application of the results of basic laboratory and clinical research to patient care and to the promotion of health. As a first step toward meeting that goal, the National Heart, Lung, and Blood Institute (NHLBI), in 1975, established three National Research and Demonstration Centers: one in heart and blood vessel diseases, one in lung diseases, and one in blood diseases and blood resources.

The National Heart, Lung, and Blood Advisory Council has periodically reviewed the original concept for National Research and Demonstration Centers. The Council has expressed concern about the inadequate amount of demonstration and education research in the United States generally and about the need to enhance the magnitude of this research effort if the number of National Research and Demonstration Centers were to be increased. In September 1980, the Council recommended that the procedure for designating and supporting future National Research and Demonstration Centers be changed. This recommendation was subsequently accepted by the NHLBI. The Council suggested that a two-phase process be instituted in the creation or designation of new Centers and that an RFA for demonstration and education research be the first phase of the process. The RFA for the first phase was released in March 1981. Although the NHLBI awarded seven grants as a result of the first competition, these awards represented only a limited number of the program areas of the NHLBI. Consequently, the National Heart, Lung, and Blood Advisory Council recommended postponing the competition for National Research and Demonstration Centers so that additional institutions could become involved in demonstration and education research. This current RFA thus represents an attempt to stimulate further interest in demonstration and education research.

IV. DEFINITIONS AND PROJECT CONTENT

The application for a demonstration and education research grant may include a demonstration research project, an education research project, or some combination of both or either. An institution may submit more than one application. Generally, a project should be designed so that it can be implemented and evaluated within a maximum of five years.

The following sections define demonstration research and education research within the context of this announcement.

A. Demonstration Research

As defined for the purpose of this RFA, demonstration research is a project designed to test the applicability of new approaches to the prevention, diagnosis, or control of diseases that have been shown to be effective in controlled laboratory or clinical investigation. These new approaches would be tested in an appropriate setting, such as defined groups within communities, physicians' offices or other health-care settings or work sites.

The development of health-significant demonstration research relevant to the goals of the NHLBI should include the following considerations:

- significance of the problem and anticipation of the expected gains in terms of health promotion, disease prevention, potential for reduction of morbidity or mortality, improvement and extension of health-care services in the community, effective use of health personnel, and enhancement of cost effectiveness;
- utilization of special features of the specific setting, such as prevalence of a particular disease, unique research resources, specific population groups suitable for the project, special health-

delivery facilities, and local health organizations, but these special features should not be so specific as to preclude appropriate generalization of the findings;

- evidence that the investigators have the experience, competence, and commitment necessary for the successful implementation of the project, that appropriate disciplines would be represented in the proposed project, that the applicant institution has the resources necessary and is committed to the proposed study, and that participating local groups have indicated their commitment to the study as proposed;
- descriptions of the theoretical and factual bases for the proposed study, research questions or hypotheses to be tested, the research design to be used, procedures for sample selection, variables to be observed, methods and materials to be used, instruments and procedures to be used for measurements, approaches to data management and analysis, methods for statistical analysis, plans for dissemination of results, and the potential for the effectiveness of the demonstration in other settings; and
- plans for evaluation that include specific procedures, instruments, and methods to be used in determining whether the objectives have been met.

B. Education Research

As defined for the purpose of this RFA, an education research project is one designed to investigate education methods for the maintenance of health, prevention of disease, or the delivery and utilization of health-care services. The development of health-significant education research relevant to the goals of the NHLBI should include the following considerations:

- clear identification of the need for a change in health behavior, including a description of the existing health behavior addressed, the anticipated course if no program is instituted, and the significance of attempting to alter behavior;
- definition of the objectives in terms of the behavioral change desired, the intervention strategies to be used, and the criteria by which change is to be measured;
- careful definition of the study population, including plans for recruitment of participants and maintenance of the stud population, any anticipated changes in the composition of [illegible] study population, and plans for measuring the impact of these changes on a project;
- descriptions of the theoretical and factual bases for the proposed study, the research questions or hypotheses to be tested, the research design to be used, procedures for sample selection, variables to be observed, methods and materials to be used, instrument and procedures to be used for measurement,

approaches to data management and analysis, and methods for statistical analysis; and

- o plans for evaluation that include specific procedures, instruments, and methods to be used in determining whether the objectives have been met.

Continuing medical education with only the goal of information dissemination does not fit these criteria.

V. RESEARCH SCOPE

The following list includes major diseases and areas of interest to the Divisions of the NHLBI. The proposed demonstration and education research projects must be related to the programs of the NHLBI, as exemplified in this list, and should capitalize on the strengths of the applicant institution. The list is neither all-inclusive nor exclusive, nor is it in an order of priority of interest.

Heart and Blood Vessel Diseases:

Risk factor or factors for coronary heart disease in children and (or) adults, including high blood pressure, elevated serum cholesterol, smoking, lack of exercise, overweight, and diabetes; nutrition as it affects the cardiovascular system; rehabilitation after a myocardial infarct; prosthetic devices related to heart and vascular diseases; atherosclerosis; hypertension; coronary heart disease; arrhythmias; heart failure and shock; cerebrovascular disease, excluding the neurological components of completed stroke; peripheral vascular disease; congenital and rheumatic heart disease; cardiomyopathy; and infections of the heart.

Lung Diseases:

Obstructive diseases of the airways; pediatric pulmonary diseases; fibrotic and immunologic interstitial lung diseases; respiratory failure; pulmonary vascular diseases; risk factors for lung disease, including smoking, occupational exposure, and environmental exposure; and maintenance of respiratory health. (Cancer of the lung, upper respiratory infections, and tuberculosis are the responsibility of other program components of the National Institutes of Health and are not included in this program.)

Blood Diseases and Blood Resources:

Thromboembolic disorder, the hemophilias; and other conditions related to the plasma clotting factors; platelet abnormalities; microcirculatory thrombosis; bone marrow physiology and dysfunction; diseases and disorders of the red blood cell, including sickle cell disease, the thalassemias, and similar disorders; optimal utilization of the national blood resource; blood and blood-component therapy; and blood banking functions. (Malignancies of the blood, as well as immunologic and other disorders of the white blood cells, are the responsibility of other components of the National Institutes of Health and are not included in this program.)

VI. MECHANISM OF SUPPORT

Grants for demonstration and education research sponsored by the NHLBI* will be awarded under the authority of the Public Health Service Act, Title III, Section 301, and Public Law 95-622, Section 415, and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. Support may also be derived in part from other sources—Federal, local, public, and private. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

The total amount of funds that will be set aside will be determined at the November 1982 meeting of the National Heart, Lung, and Blood Advisory Council. It is anticipated that there may be from eight to twelve projects awarded at a total cost of about $2,000,000. The specific amount to be funded will, however, depend on the merit and scope of the applications received and the availability of funds.

While each applicant institution is expected to develop its own program in accordance with local expertise, interests, and resources, each must be willing to work with the other grantees in furthering the goals of the NHLBI.

VII. REVIEW PROCEDURES AND CRITERIA

Upon receipt, applications will be reviewed for their responsiveness to the specific objectives described in this announcement. An application judged to be unresponsive will be returned to the applicant. If a proposal submitted in response to this RFA is identical to a grant application already submitted to the NIH for review, the applicant will be asked to withdraw the pending application before the new one is accepted. Simultaneous submission of identical applications will not be allowed.

The Division of Extramural Affairs, NHLBI, will manage the scientific and technical merit review of applications. The initial peer review will be conducted by consultants who have expertise in each area of the proposed program. The subsequent review will be by the National Heart, Lung, and Blood Advisory Council.

The peer review of demonstration and education research projects will include assessment of the following:

- o scientific merit of the research project, the importance of the underlying disease or health-related issue, and the relevance to the objectives of the RFA;
- o soundness of the project design and of the procedures that would be used;

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*The demonstration and education programs that the NHLBI intends to support are related to the provisions of the National Heart, Blood Vessel, Lung, and Blood Act of 1972 (Public Law 92-423), as extended by the Health Research and Health Service Amendments of 1976 (Public Law 94-278), the Biomedical Research Extension Act of 1977 (Public Law 95-83), and subsequent reauthorizations through 1980, and are described in the 1981 Catalog of Federal Domestic Assistance, program numbers 13.837, 13.838, and 13.839.

- experience, commitment, and leadership ability of the principal investigator and the qualifications and experience of the other responsible investigators to do the proposed research;
- reasons for selection of the study population or populations, and, for the education project, the significance of attempting to alter existing health-related behavior;
- availability of necessary resources and the commitment of local population groups to cooperate and participate;
- plans for evaluation of the progress and of the effect of a project;
- plans for the collection, storage, retrieval, and analysis of data related to a project;
- strength of the management plan for assuring the smooth functioning of a project, including
  - an administrative and organizational structure that would facilitate attainment of the proposed objectives of a project, the availability of appropriate consultants, and
  - a plan for the maintenance of quality control in all aspects of a proposed project;
- availability of necessary physical, professional, and community resources to support a project and to successfully develop and maintain working relationships with the relevant segments of the community; and
- a willingness to exchange experience and information with other investigators involved in demonstration and education research projects, if appropriate, and with the NHLBI.

VIII. METHOD OF APPLYING

NOTE:

Applicants are urged to consult with appropriate members of the staff of the NHLBI before and during the preparation of their applications regarding questions of policies, procedures, and guidelines.

Letter of Intent

Applicants should submit a letter of intent to the NHLBI not later than August 2, 1982. The NHLBI requests such letters so that the staff can plan for the review. A letter of intent is not binding and will not be considered in the review of any application submitted subsequently.

The letter should be addressed to:

Jerome G. Green, M.D.
Director, Division of Extramural Affairs
National Heart, Lung, and Blood Institute
National Institutes of Health
Westwood Building, Room 7A17
Bethesda, Maryland 20205

Format for Applications

The format for applications is that of the form PHS 398. Please refer to the Instruction Sheet for PHS 398 (Revised 5/80) for specific directions. In addition to the sections specified in the form PHS 398, applicants must include the following information, as appropriate:

- Title page

  Complete this page in the same manner as for a research grant application. Type in item 2: "NHLBI Demonstration and Education Research - RFA NIH-NHLBI-82G-3."

- Ongoing research and relation to proposed project

  Describe concisely the institution's ongoing basic and clinical research related to the general area of the proposed demonstration or education project.

  Explain briefly the actual or potential value these ongoing basic and clinical research programs have or would have for the proposed demonstration or education research.

- Description of the study population

  Describe and define the study population or populations for the demonstration and education research in sufficient detail to provide a clear understnding of the scope of a project and its potential for general application.

  Describe the status of health services, health education activities, and disease areas in the study population if relevant to the proposed project.

- Patient and subject availability

  Provide evidence for the availability and commitment of patients and subjects. This is particularly important for demonstration, prevention, and control efforts that may require cooperation with community physicians and collaboration with existent community health programs.

- Organization and administration

  Describe any relation of the proposed research to other relevant programs within the sponsoring institution.

- Capability of staff

  Describe how the staff would fulfill the needs for the different kinds of expertise and capability required to accomplish the proposed study.

- Facilities

  Describe facilities available for the proposed research, including, if appropriate, facilities of other collaborating institutions. Describe new facilities necessary for the proposed research and state how they would be obtained. (NHLBI funds to support construction are not available at the present time.)

  Describe the geographic distribution of space and personnel and the plans for coordination of efforts in central and outlying facilities. Geographic proximity is desirable, but not mandatory, for demonstration and education research projects.

Application Procedure

The completed application and six (6) signed, exact photocopies of it should be sent or delivered to:

Division of Research Grants
National Institutes of Health
Westwood Building Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205

In addition, please send eighteen (18) copies to:

Review Branch
Division of Extramural Affairs
National Heart, Lung, and Blood Institute
Westwood Building Room 5A-10
5333 Westbard Avenue
Bethesda, Maryland 20205

Applications must be received by October 15, 1982.

Label the outside of the mailing package and item 2 of the face page of the application "NHLBI Demonstration and Education Research - RFA NIH-NHLBI-82G-J."

Indicate in a brief covering letter that the application is being submitted in response to this RFA: "Demonstration and Education Research in Heart, Blood Vessel, Lung, and Blood Diseases and Blood Resources." Send a copy of the letter to Dr. Jerome G. Green at the address given under the section entitled "Letter of Intent."

Timetable

Letter of intent	August 2, 1982
Receipt of applications	October 15, 1982
Advisory Council review	May 19-21, 1983
Earliest possible start date	July 1, 1983

Inquiries

Inquiries about demonstration and education research in heart and blood vessel diseases may be addressed to:

Dr. Barbara Packard
Director
Division of Heart and Vascular Diseases
National Heart, Lung, and Blood Institute
National Institutes of Health
Federal Building Room 416
Bethesda, Maryland 20205

Telephone: (301) 496-2553

Inquiries about demonstration and education research in lung diseases may be addressed to:

Dr. Suzanne Hurd
Acting Director
Division of Lung Diseases
National Heart, Lung, and Blood Institute
National Institutes of Health
Westwood Building Room 6A15
Bethesda, Maryland 20205

Telephone: (301) 496-7208

Inquiries about demonstration and education research in blood diseases and blood resources may be addressed to:

Dr. Amoz I. Chernoff
Director
Division of Blood Diseases and Resources
National Heart, Lung, and Blood Institute
National Institutes of Health
Federal Building Room 516
Bethesda, Maryland 20205

Telephone: (301) 496-4868

ANNOUNCEMENT

THE AVAILABILITY OF OPPORTUNITIES FOR AMERCIAN SCIENTISTS TO PERFORM COLLABORATIVE RESEARCH OUTSIDE THE UNITED STATES

FOGARTY INTERNATIONAL CENTER

The John E. Fogarty International Center for Advanced Study in the Health Sciences (FIC) of the National Institutes of Health announces the availability of postdoctoral fellowships to U.S. health scientists who wish to conduct collaborative research abroad. The purpose of these fellowships is to enhance the exchange of research experience and information in the various biomedical and behavioral sciences. The types of activity that are supported by these programs include collaboration in basic or clinical research, and the familiarization with or utilization of special techniques and equipment not otherwise available to the applicant. Applications having any of the following as the major feature cannot be accepted: brief observational visits, attendance at scientific meetings, attendance in formal training courses, or independent research projects within the host country.

PROGRAMS

Five programs are available to U.S. citizens or permanent residents:

SENIOR INTERNATIONAL FELLOWSHIP (SIF)
(Supported and administered by the FIC)

SWEDISH MEDICAL RESEARCH COUNCIL FELLOWSHIPS (SMRC)
(Supported by the Government of Sweden)

SWISS NATIONAL SCIENCE FOUNDATION POSTDOCTORAL FELLOWSHIPS (SNSF)
(Supported by the Government of Switzerland)

FRENCH NATIONAL INSTITUTE OF HEALTH AND MEDICAL RESEARCH (INSERM)
POSTDOCTORAL FELLOWSHIPS
(Supported by the Government of France)

NIH-FRENCH NATIONAL CENTER FOR SCIENTIFIC RESEARCH PROGRAM
FOR SCIENTIFIC COLLABORATION (CNRS)
(Under an agreement between the NIH and the CNRS, the two organizations share in the support of U.S. and French scientists to work at laboratories in France and the U.S., respectively.)

ELIGIBILITY REQUIREMENTS

Applicants must meet the following requirements:

U.S. citizen or permanent U.S. resident;

doctoral degree in clinical, behavioral or biomedical science;

ten years or less or postdoctoral experience;
(SIF applicants should have five years or more postdoctoral experience, not so specified for the CNRS)

professional experience in the health sciences for at least two of the last four years (not so specified for the CNRS);

affiliated with a U.S. public or private nonprofit research, clinical or educational institution (only required for SIF).

APPLICATION AND SELECTION

Applications for these programs are reviewed once a year. The receipt date for applications to the FIC Senior International Fellowship Program is June 1, 1982. The receipt date for all other applications is October 1, 1982. All applications are reviewed for scientific merit by the National Institutes of Health. The organization which provides financial support of the program selects candidates for participation. While the maximum period of support for all programs is one year, the minimum period of support varies with each program.

Information and applications are available from:

International Research and Awards Branch
Fogarty International Center
National Institutes of Health
Bethesda, Maryland 20205

Prospective applicants for the Senior International Fellowship Program, the FIC sponsored program, may obtain information brochures from the above address. Only the office of the dean or equivalent institutional official may request SIF fellowship applications which will be available until May 15, 1982.

All correspondence should refer to specific programs and must be clearly marked using one of the following:

Senior Fellowships
Swedish Fellowships
Swiss Fellowships
INSERM
CNRS

For an expeditious reply, please send a self-addressed label with your request.

NONHUMAN PRIMATES AVAILABLE

The National Institutes of Health has established supply sources of nonhuman primates for the National Institutes of Health (NIH) and Alcohol, Drug Abuse and Mental Health Administration (ADAMHA) supported projects. Production colonies of rhesus (Macaca mulatta) and cynomolgus (Macaca fascicularis) monkeys have been established. Priority is given to investigators with NIH or ADAMHA supported projects. Other investigators in nonprofit institutions are invited to submit requests for primates for use in biomedical and behavioral projects. All requests should be in letter form and indicate the source of support; and if NIH or ADAMHA, include the title, number and principal investigator of the grant or contract. The request should also include the specifications for the animals required, including number, age, sex or other special characteristics. The entire request need not exceed one typewritten page. All inquiries should be addressed to:

Dr. Carl E. Miller
Building 31, Room 5B59
National Institutes of Health
Bethesda, Maryland 20205

Telephone: (301) 496-5175

The price indicated for each animal includes shipping costs within the continental United States. The funds will be paid directly to the contractor supplying the animals to partially offset the cost of the NIH-supported breeding program. Other inquiries are invited.

Animals currently available are as follows:

Normal rhesus monkeys (Macaca mulatta)

	Price
100 females - colony born - 1981	$750
150 males - colony born - 1981	750
30 males - colony born - 1980	850
2 females - colony born - 1979	950
1 female - colony born - 1978	950
Pregnant females - wild-caught colony production stock as available during reproductive season, gestation estimated ± 15 days -	$1,200 each
Specific mating dates -	1,500 each
Retired breeders - as available	850

Normal colony produced cynomolgus monkeys (Macaca fascicularis)

10 females - colony born - 1981	$350
33 males - colony born - 1981	350
11 males - colony born - 1980	400
27 males - colony born - 1979	400
3 males - colony born - 1978	400
2 males - colony born - 1977	400
14 females - reproductive culls	300
2 males - reproductive culls	300

Prices include delivery in the continental United States.

The above prices are for nonprofit institutions.

NOTICE

AVAILABILITY OF AGED MONKEYS (MACAQUE SPECIES)

NATIONAL INSTITUTE ON AGING

The National Institute on Aging (NIA), National Institutes of Health (NIH), through an Intra-Agency Agreement with the NIH Division of Research Resources (DRR), has established set-aside colonies of aging monkeys. At any of four DRR-supported Regional Primate Research Centers (PRC), collaborating investigators, visiting scientists, and graduate and postgraduate students supported by NIA grants and awards can use the nonhuman primates for gerontological and geriatric research programs.

OBJECTIVES

Objectives of the program are:

1. To provide a research and research training resource for biological, behavioral, social, and clinical studies on the processes, conditions, and characteristics relevant to the aging process, and the diseases and other special problems of aged humans;
2. To determine which gerontological and geriatric research problems are best pursued with nonhuman primates;
3. To supply biological specimens to investigators performing research on the aging process.

AVAILABLE RESOURCES

ANIMALS

The following animals are available for use primarily in experiments which will not cause any long-term or irreversible damage to the animals. However, at centers where aged animals can be replaced from the breeding colony or other sources, some animals may be used for high-priority terminal experiments.

Primate Center	Species	# of Animals	Range of Birth Years
California	M.mulatta	55	1964-67
Oregon	M.mulatta	49	1961-67
Washington	M.nemestrina	27	1957-67
Wisconsin	M.mulatta	56	1956-67

Complete experimental and clinical histories of these animals are on record at the respective PRCs. An independent panel of primatologists and comparative pathologists has selected the monkeys for inclusion in the set-aside colonies from a pool of 360 monkeys, 15 years old or older, on the basis of their experimental and clinical histories. Animals which had experienced such severe interventions as whole body Cobalt-60 exposure, amygdalectomy, or isolation rearing were judged unsuitable for the set-aside colonies. In contrast, animals that had been breeders, or had been exposed to short-acting drugs, or to interventions with expected local or mild effects, were judged suitable.

At present, the major research emphases of the four centers are as follows:

- The main research orientation of the Oregon Regional Primate Research Center, Beaverton, Oregon is in reproductive biology. Other research emphases include cardiovascular and metabolic research, immunology, cutaneous biology, biochemistry, nutrition, and behavior.
- The Regional Primate Research Center at the University of Washington, Seattle, Washington emphasizes developmental biology, neurosciences and behavior, cardiovascular function, disease models, endocrinology and metabolism, and immunogenetics.
- Interactions among hormones, social environment and the brain, and how these factors influence reproductive functions in nonhuman primates are the principal research foci at the Wisconsin Regional Primate Research Center, Madison, Wisconsin.
- The California Primate Research Center at Davis, California, is engaged in studying the effects of environmental factors on nonhuman primates, perinatal biology and reproduction, respiratory diseases, infectious diseases and immunology, and behavioral biology.

SERVICES

Certain services may be provided to NIA grantees by the four PRCs. Investigators interested in availing themselves of these services should contact the Director(s) of the appropriate PRC(s), and negotiate agreements for specific services or collaborative research arrangements prior to submitting a new, renewal, or supplemental research grant application. Appropriate documentation of all such agreements should be appended to the grant application.

Tissue specimens, organs, blood, skeletal structures, viral specimens and other biological samples from these animals may be provided to NIA grantees when available. Such specimens are collected by non-invasive, or minimally damaging techniques.

In most cases, the aged animals should be maintained on location at the respective PRC for the duration of the grant. Under rare circumstances, at the discretion of the Head, Aging Primate Research Resource Program, NIA, and Director of the relevant PRC, however, arrangements may be possible for purchase and transfer of a small number of animals by the grantee institution. Negotiation for purchase of aging animals should be made with the Director of the PRC and coordinated through the Head, Aging Primate Research Resource Program, NIA.

The following guidelines should be used in applying for use of the aging monkey resources. The grant application, whether new, renewal, or supplemental, should be coordinated with the appropriate PRC Director to insure that:

- the experimental protocol is appropriate to that facility;
- the necessary animals, equipment, services, and space are available;
- supplies/equipment essential for the studies can be designated;
- facilities are available for the proposed studies; and
- the timing of the studies is not disruptive to the ongoing PRC activities.

Grant applicants should request use of the aged primate resources via the standard research grant form (PHS Form 398) submitted to the Division of Research Grants for review of scientific merit. The grant application should include verification that the above criteria have been met.

Applicants should include itemized budgets for all costs related to maintenance (per diem) and experimental use of the animals. Such itemized costs should include charges for research-related services which may be procured from the Center. All fees (e.g., technical sevices, animal purchases) should be pre-determined through discussions with the PRC Director and documented in the grant application. If transfer of animals to the grantee institution is necessary, costs of the purchase, transfer, per diem maintenance, and related services should be included in the budget of the grant application.

If the requested animal or services are for use in pilot studies by current NIA grantees, the following information should be submitted to Ms. Jane Soban at the Aging Primate Research Resource Program, National Institute on Aging:

- proposed research protocol and its relevance to aging (4 copies);
- recent publications related to proposal (2 copies);
- curriculum vitae (4 copies); and
- appropriate documentation of agreement with the PRC Director(s).

Upon receipt of this request, and necessary additional materials, the proposal will be sent for review of scientific merit.

SOURCES OF FURTHER INFORMATION

Information pertaining to the research areas, facilities and service of the PRCs are published in the Animal Resources Directory of the DRR. A copy of this may be obtained from:

Office of Science and Health Reports
Division of Research Resources
Building 31, Room 5B-13
Bethesda, Maryland 20205

For further information contact:

Head, Aging Primate Ressearch Resource Program
National Institute on Aging
National Institutes of Health
Bethesda, Maryland 20205

Telephone: (301) 496-6402

Director, California Primate Research Center
University of California
Davis, California 95616

Telephone: (916) 752-0420

Director, Oregon Primate Research Center
505 N.W. 185th Avenue
Beaverton, Oregon 97005

Telephone: (503) 645-1141

Director, Washington Primate Research Center
University of Washington
Room I-421 - Health Sciences Bldg. J-50
Seattle, Washington 98195

Telephone: (206) 543-1430

Director, Wisconsin Regional Primate
Research Center
University of Wisconsin
1223 Capitol Court
Madison, Wisconsin 53706

Telephone: (608) 263-3500

ANNOUNCEMENT

PREVENTIVE ONCOLOGY ACADEMIC AWARD (POAA)

NATIONAL CANCER INSTITUTE

I. BACKGROUND OF POAA

A. The National Cancer Institute invites competition for Preventive Oncology Academic Awards. Each School of Medicine, Osteopathy, Dentistry, Public Health, or NCI-designated cancer center in the United States and its possessions or territories is eligible to compete for one non-renewable Preventive Oncology Academic Award for a project period not to exceed five years. The number of new awards made each year will depend on the availability of funds.

B. The Preventive Oncology Academic Award Program is intended to stimulate high quality research on which educational programs oriented toward cancer prevention could be based in schools which do not have such programs or to strengthen the research and education programs of schools in which high quality research in preventive oncology already exists. It is expected that each program in cancer prevention will build upon the institution's demonstrable expertise and experience in epidemiology, human genetics, biostatistics, clinical oncology, nutrition and other pertinent basic cancer research.

C. The Preventive Oncology Academic Awards, which are made on the basis of nationwide competition, are available to individual investigators with academic teaching and/or research appointments in their respective institutions. POAA's support these individuals for needed research and educational objectives and development, implementation, and/or improvement of a preventive oncology curriculum.

II. DEFINITION OF PREVENTIVE ONCOLOGY

For purposes of Preventive Oncology Academic Awards (POAA), preventive oncology is mainly concerned with etiologic studies and the primary prevention of cancer. In certain instances it may be appropriate to evaluate the efficacy of preventive measures.

III. OBJECTIVES OF THE AWARD

The Preventive Oncology Academic Award, which is made on the basis of nationwide competition, is available to:

This program is described in the Catalog of Federal Domestic Assistance No. 13.393, Cancer Cause & Prevention Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

1. Support an outstanding individual faculty member for:

    a. participation in research experiences related to preventive oncology

    b. enhancing relevant scientific skills if a need is demonstrated

    c. strengthening or implementing a preventive oncology curriculum and the research program on which it should be based.

2. Provide superior learning opportunities to students enrolled in the institution through their exposure to research and to courses relevant to preventive oncology.

3. Facilitate exchange of ideas and methods among institutions and centers with special interest and expertise in preventive oncology.

IV. CRITERIA FOR THE POAA

Competitive review for a Preventive Oncology Academic Award will assess the plans of both (a) the sponsoring institution and (B) the proposed candidate.

A. THE INSTITUTION MUST:

1. Select and sponsor a candidate with: (a) demonstrated competence in preventive oncology, as well as (b) a major career interest in research and educational programs. The candidate must be a citizen, a noncitizen national of the U.S., or have been lawfully admitted to the U.S. for permanent residence.

2. Provide the candidate with: (a) the opportunity to acquire the professional skills for which need is demonstrated, and (b) adequate time to develop or improve the preventive oncology program.

3. Present institutional plans for the preventive oncology program which is to be developed under support of the POAA: (a) these plans must state the program's objective in terms of measurable outcomes and provide benchmarks aginst which progress is to be measured. (b) the plan should clearly distinguish between any ongoing activities and those to be accomplished as a result of the POAA, outlining the relationship between the proposed plan and related teaching and research programs of the institution.

4. Identify and demonstrate availability of resources (e.g., populations, patients, manpower, materials) necessary to implement the proposed program.

5. Provide access to physical facilities (e.g., computer, laboratory, clinical, classroom office facilities) for rigorous preventive oncology research.

6. Provide written evidence of commitment from the administration, and chairperson(s) of sponsoring department(s) and curriculum committee to the implementation and/or further development of the proposed program.

7. Propose mechanisms for continued institutional support of the preventive oncology program, following the award period.

B. THE CANDIDATE MUST:

1. Hold a doctoral degree or its equivalent from an accredited institution (e.g., D.D.S., D.O., Dr.P.H., D.V.M., M.D., Ph.D.);

2. Possess an appropriate teaching and/or research appointment in the sponsoring institution at the time the award is activated;

3. Have sufficient training and experience so that no more than two years of intensive supplemental preparation is needed to meet minimal POAA requirements. These requirements include:

   a. demonstrated competence in: biomedical research relevant to cancer prevention, including epidemiology and/or human genetics, clinical oncology and biostatistical research methods, plus

   b. substantive knowledge of: cancer epidemiology and prevention, carcinogenesis research, health service delivery systems, public health regulation and practice, as well as medical education procedures and administration.

4. Specify a program for enhancing personal skills as needed, e.g., further education in epidemiology, biostatistics, genetics, nutrition, clinical oncology and/or other pertinent areas of research in cancer etiology and prevention.

5. Present a program: (a) for developing or improving preventive oncology research and education in the grantee institution, and (b) for evaluating the outcome of the effort. This program should include detailed plans including the proposed curriculum, course description and syllabi, where appropriate.

6. Commit a substantial portion of time and effort to preventive oncology research and to the proposed programs.

7. Submit an annual program performance report along with the continuation support application (Type 5).

8. Agree to meet annually with other recipients of POAA's to exchange ideas, methods and program evaluations, as specified in the POAA objectives. The meeting is to be sponsored by the National Cancer Institute, with travel costs borne by POAA grant.

V. PROVISIONS OF THE PREVENTIVE ONCOLOGY ACADEMIC AWARD (POAA)

A. Within available funds, and consonant with the objectives of the POAA, and with satisfactory progress, the Institute will provide funds annually for a project period up to five years. This award is non-renewable.

B. The POAA funds may be used for:

1. Personnel: salary support for candidate and all other personnel, in direct proportion to the effort expended on the P.O. program, to include, e.g., P.O. assistants and associates; curriculum specialists and other faculty; as justified and specified by level of professional development; and in accordance with institutional policy.

2. Consultants costs: for a limited number of experts in the areas of P.O. research and education.

3. Equipment: necessary to develop P.O. curriculum.

4. Supplies by category: necessary to achieve P.O. program objectives.

5. Travel: domestic travel to other institutions and meetings to enable the candidate to develop essential skills, and also to meet with other candidates to exchange ideas, methods, and program evaluations. (See IV. B-9).

6. Other expenses may include: (a) stipend, tuition and fee costs related to the implementation by the candidate of a proposed program for enhancement of personal skills; (b) computer costs, teaching aids, materials and books relevant to the development of the P.O. program, and, (c) postage, copying costs, telephone costs.

C. The POAA funds may not be used for: patient care costs, alterations and renovations, and contractual or third party payment costs. These are ineligible categories for support under the POAA grant mechanism.

D. Limited funds, if requested, may be used at the discretion of the candidate to support short term research or teaching experiences in preventive oncology. Such experiences may be (1) designed to educate faculty or students in principles and techniques of preventive oncology research or (2) feasibility studies integral to research planning.

VI. REVIEW OF APPLICATIONS

Applications for initial Preventive Oncology Academic Awards will be appraised in terms of criteria outlined for the institution and the candidate in Section IV, "Criteria for the Preventive Oncology Academic Award." Applications will be evaluated by an appropriate NCI peer review group.

VII. METHOD OF APPLYING

1. The annual receipt date for POAA applications will be September 1.

2. The requested begin date for funding should be July 1 of the following year.

3. Application forms (PHS 398, Revised 5/80) may be obtained from the institution's application control office. If not otherwise available, they can be requested from:

Office of Grants Inquiries
Division of Research Grants
National Institutes of Health
Room 448 Westwood Building
5333 Westbard Avenue
Bethesda, Maryland 20205

4. Type the phrase "PREVENTIVE ONCOLOGY ACADEMIC AWARD" as the title for the proposal on the front page of the application. Use the Special Guidelines for preparation of a Preventive Oncology Academic Award. These and limited staff consultation relating to eligibility and appropriate areas of emphasis may be obtained from:

Special Programs Branch
National Cancer Institute
National Institutes of Health
Room 8C16 Landow Building
7910 Woodmont Avenue
Bethesda, Maryland 20205

Telephone: (301) 496-9600

ANNOUNCEMENT

DIETARY SODIUM AND ITS ROLE IN THE PREVENTION AND MANAGEMENT OF HYPERTENSION

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

The National Heart, Lung, and Blood Institute (NHLBI) supports a variety of research programs related to the prevention, treatment, and control of hypertension. Since this broad area of research is important to several programs in the Division of Heart and Vascular Diseases (DHVD) of the Institute, the present program announcement is being issued from the Division. A program announcement is designed to focus attention upon a topic or problem. Applications will be considered as applications for the regular research grant program, without special set-aside funds.

The objective of this program announcement is to encourage the submission of scientifically meritorious applications concerning a broad range of investigations, including physiological, clinical, preventive, and therapeutic research, regarding the role of dietary sodium in hypertension and the prevention of hypertension.

It is estimated that 35 million persons in the United States have high blood pressure. This fact, coupled with recent evidence from the Hypertension Detection and Followup Program that significant reductions in mortality can result from sustained drug treatment of high blood pressure, makes research into the role of dietary sodium in the prevention and management of high blood pressure of special interest. This research area has been identified by the Salt and Water Subgroup of NHLBI's Hypertension Task Force, the NHLBI Clinical Applications and Prevention Advisory Committee and the Arteriosclerosis, Hypertension, and Lipid Metabolism Advisory Committee as needing emphasis.

Examples of needed research include studies of:

- The relationship between sodium and weight.
- The interrelationship of sodium and weight.
- Sodium sensitivity.
- Salt appetite.
- Methodology for determining sodium intake in humans.

This program is described in the Catalog of Federal Domestic Assistance No. 13.837, Heart and Vascular Diseases Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 73-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

Investigations that take account of other dietary factors, caloric intake, and energy expenditure are encouraged.

The above list is intended to provide examples only and does not preclude the submission of applications involving other research approaches to the issues under consideration. In addition, this program announcement is not intended to discourage investigators from their pursuit of promising ideas in related or unrelated topics.

Application Submission and Review

Application receipt dates for new applications are the regular application receipt dates of July 1, November 1, and March 1. Applications received after any one receipt date are considered and reviewed together with those received by the next receipt date. The earliest possible award date is approximately nine months after the receipt date. Applicants should use the regular research grant application form PHS-398, which is available at the applicant's institutional application control office or from the Division of Research Grants, NIH.

In order to identify the response to this announcement, check "yes" and put "Dietary Sodium/Hypertension" under item 2 on page 1 of those grant applications relating to the topics identified herein. The completed application should be mailed to:

Division of Research Grants
National Institutes of Health
Westwood Building Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205

The Division of Research Grants will assign applications to study sections for review according to the NIH process for regular research grant applications. Approved applications will compete for available funds with all other approved grant applications assigned to the NHLBI. Additional information may be obtained by contacting:

Marilyn Farrand, R.D.
Preventive Cardiology Branch
Division of Heart and
Vascular Diseases
National Heart, Lung, and
Blood Institute
National Institutes of Health
Federal Building Room 6A08
7550 Wisconsin Avenue
Bethesda, Maryland 20205

Telephone: (301) 496-3503

Armando Sandoval
Hypertension Branch
Division of Heart and
Vascular Diseases
National Heart, Lung, and
Blood Institute
National Institutes of Health
Federal Building Room 4C08
7550 Wisconsin Avenue
Bethesda, Maryland 20205

Telephone: (301) 496-1857

ANNOUNCEMENT

PHARMACOLOGY PROGRAM

NATIONAL INSTITUTE ON AGING

I. INTRODUCTION

The National Institute on Aging (NIA) was established in 1974 for the "conduct and support of biomedical, social and behavioral research and training related to the aging process and the diseases and other special problems and needs of the aged." Under this broad mandate, it has encouraged and supported a diversified research program related to aging.

Drug manufacturers routinely test new drugs and determine safe dose levels in healthy, young adults. The largest degree of drug use, however, is among the elderly, who often respond differently to drugs than do young adults. Definitive information is needed to elucidate the mechanisms underlying differences in response between young adults and the elderly and also to provide optimal drug dosage levels for elderly patients.

The increased incidence of multiple diseases among the elderly often leads to the use of combinations of drugs. The effect of such polypharmacy can be undesirable and have potentially dangerous side effects. It is important to learn more about interactions between various drugs as well as interactions between drugs and disease states and nutritional status.

Clinical and basic research to gain fundamental knowledge on the nature and causes for differences in the response of the elderly to drugs represents an important element of NIA's responsibility. The Pharmacology program, a part of Biomedical Research and Clinical Medicine, NIA, is specifically concerned with research and training in this area.

II. BACKGROUND

Increased interest by the research community in gerontological pharmacology is strongly encouraged. The following sources of background information may be useful to investigators new to this area.

(1) Steinberg, G.M. and Schneider, E.L.: NIA Second Workshop on Pharmacology and Aging, June, 1981. The Pharmacologist 24: Issue No. 2 (1982).

This program is described in the Catalog of Federal Domestic Assistance No. 13.866, Aging Research. Awards will be made under the authority of the Public Health Service Acts, Sections 301 (Public Law 78-410, as amended; 42 USC 241) and 472 (42 USC 2891-1) and administered under PHS grants policies and Federal Regulation 42 CFR Parts 52 and 66 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

(2) Vestal, Robert E.: Drug Use in the Elderly: A Review of Problems and Special Considerations. Drugs 16:358-382 (1978).

(3) Crooks, J. and Stevenson, I.H.: Drugs and the Elderly. Perspectives in Geriatric Clinical Pharmacology. University Park Press, Baltimore, Maryland, 1979.

(4) Conrad, K.A. and Bressler, R.: Drug Therapy for the Elderly. C.V. Mosby Co., St. Louis, 1982.

(5) Plein, J.B. and Plein, E.M.: Aging and Drug Therapy. Annual Review of Gerontology and Geriatrics (Volume 2), edited by Eisdorfer C., Springer, New York, 1981.

III. GOALS AND SCOPE

A major goal of the NIA is to identify changes in pharmacological responses that occur with aging and to elucidate the basic mechanism involved. This information should lead to development of more appropriate and efficacious therapy, to reduction of adverse drug side effects and to prevention of iatrogenic disease.

IV. SPECIFIC OBJECTIVES

The NIA seeks research and research training grant applications in gerontological and geriatric pharmacology. Investigations are encouraged on the aging process (beyond maturity) in all of the physiological systems that are subject to pharmacological intervention. Among possible approaches are clinical studies of healty and diseased elderly persons and more basic studies in experimental animals. Appropriate topics include, but are not limited to, the areas noted below. These areas are not listed in any order of priority.

Areas of Greatest Needs or Opportunities

General: Drug actions on the peripheral and central nervous systems, and on the cardiovascular system. Effects of drugs and modulators on the immune system and on bone metabolism.

Prevention and treatment of common diseases and disorders of the elderly. Examples include: dementias, osteoporosis, decubitus ulcers, arthritis, incontinence, infection, and cancer.

Basic Pharmacology

Basic and clinical pharmacological research which leads to increasing fundamental knowledge on how and why the elderly differ from younger people in their response to drugs. Emphasis on research having a pharmacodynamic basis is encouraged. Studies of the pharmacokinetic behavior of drugs are encouraged only where there are direct and clear relationships to problems of drug action or to important physiological or homeostatic processes.

Clinical Studies

Evaluation of individual drugs to provide definitive guidance for their use in the elderly. Information to be obtained should include: proper dosage levels, effectiveness, side effects, interactions with other drugs, interactions with other disease states, nutritional status, etc.

V. SUPPORT MECHANISMS

All of the traditional NIH support mechanisms, e.g., research project grants, program projects, institutional National Research Service Awards, etc., are available for this program. For applicants interested in pilot studies and for those new to gerontological research, consideration may be given to the NIA Small Grants and Special Initiatives awards.

VI. AVAILABILITY OF EXPERIMENTAL ANIMALS

Colonies of laboratory mice, rats and monkeys for aging research are maintained by the NIA. Applicants interested in using these resources must contact (prior to submitting application) the Office of Biological Resources and Resources Development, NIA (Telephone: (301) 496-6402). Note that limited numbers of experimental animals may be made available for preapplication pilot studies.

Where the use of animal models is proposed, the appropriateness of the model should be considered and discussed in the application. The availability of specific species and strains from the NIA does not necessarily imply that these are appropriate for all research purposes.

VII. GENERAL

Applications in response to this announcement should be submitted on a standard NIH application form following the instructions contained in the NIH application packet. Type "NIA Pharmacology Program" on fact page of application. Note that clinical studies may be for research purposes only (this program does not support services) so that only those patient costs that are clearly for research components are appropriate budget items.

Inquiries may be directed to:

George M. Steinberg, Ph.D.
Pharmacology Program
Building 31 Room 5C-23
National Institute on Aging
National Institutes of Health
Bethesda, Maryland 20205

Telephone: (301) 496-1033

ANNOUNCEMENT

GERIATRIC MENTAL HEALTH ACADEMIC AWARDS

**NATIONAL INSTITUTE OF MENTAL HEALTH
(ALCOHOL, DRUG ABUSE, AND MENTAL HEALTH ADMINISTRATION
PUBLIC HEALTH SERVICE)**

BACKGROUND

The serious mental health problems of the increasing elderly population are now being identified as issues for systematic multidisciplinary research. The number of investigators in the area is small, however, and faculty to supervise geriatric mental health is limited. As the National Institute of Mental Health (NIMH) support of research in the mental health of the aging accelerated in the late 1970s, the need for investigations in psychiatry and psychiatric nursing became apparent. To address this need, NIMH is initiating a program to foster the growth of academic investigation and to recruit and prepare faculty dedicated to research and teaching in geriatric mental health.

PURPOSE

The purpose of this award is to assist in the development of a research-oriented resource person in geriatric mental health in academic settings. Upon completion of the award, the nominee is expected to function as (1) a researcher in geriatric mental health; (2) a developer of other researchers with interests in geriatric mental health; and (3) an introducer of research findings in geriatric mental health to other clinical teachers and researchers in the academic setting. This Academic Award will support an experienced faculty member, who is a psychiatrist or psychiatric nurse, in the development of necessary expertise in the research aspects of aging and mental health. This award, made to an institution, provides a superior candidate with opportunity for up to 3 years of special study and supervised experience to prepare the individual to assume a faculty leadership role in geriatric mental health.

The Academic Award is designed to provide support for individuals with high potential for academic research careers in geriatric mental health. The Academic Award differs from the Research Scientist Development Award in that the nominee is expected to assume leadership in teaching and to be a research resource as well as researcher, while the Research Scientist is expected to be a full-time research investigator. The Academic Award differs from the Individual National Research Service Award in that the focus goes beyond pure preparation in research to the development of an institutional resource.

This program is described in the Catalog of Federal Domestic Assistance No. 13.242, Mental Health Research Grants. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

ELIGIBILITY

For purposes of this announcement, eligible applicants are either:

- a U.S. college or university school of medicine, department of psychiatry, or
- a U.S. college or university school of nursing which offers a general baccalaureate program and a graduate program leading to a master's degree with a major emphasis on psychiatric nursing.

Also,

- the applicant professional school must be accredited.

Qualifications of the Nominee include:

- Evidence of research potential as shown by past training in research design and methodology, course work in these areas, involvement in research projects as scientific staff or principal investigator, participation in special research seminars or workshops, publication of research papers or monographs, or presentation of research papers at scientific meetings.
- Full-time appointment to the faculty or eligibility for full-time appointment and a guarantee of employment upon award of a grant.
- Minimum of 2 years of successful teaching experience at the applicant institution or in a similar academic program. (Priority will be given to nominees holding associate or full-professor status.)
- Psychiatry Geriatric Mental Health Academic Award nominees must have completed psychiatry residence training and be board-certified or board-eligible.
- Psychiatric Nursing Geriatric Mental Health Academic Award nominees must have at least a master's degree with a major emphasis on psychiatric nursing; priority will be given to nominees holding a doctorate.
- Priority will be given to nominees with 2 or more years of clinical experience in their respective disciplines.
- Nominees must be United States citizens or must have been lawfully admitted to the United States for permanent residence.
- Grants are not awarded under this program to support doctoral study.

TERMS AND CONDITIONS OF SUPPORT

Grants funded under this announcement are awarded directly to the academic institution. The award is made for a particular institution and individual and is not transferable to either the Geriatric Mental Health Academic Award nominee or the recipient institution. The applicant is the institution, although the Geriatric Mental Health Academic Award nominee must participate in preparing the application.

Awards will be limited to one (1) per professional school (i.e., department of psychiatry and/or school of nursing). The period of support for an individual receiving the Geriatric Mental Health Academic Award is up to 3 calendar years.

A maximum of $30,000 (exclusive of fringe benefits) per year of grant funds may be requested from NIMH for the salary of the academic awardee. The annual salary must be based upon a full-time, 12-month faculty appointment and must be consistent with the established salary level for comparable faculty positions at the applicant institution. Salaries in excess of $30,000 may be supplemented by the grantee. Any supplemental funds, however, must be from non-Federal sources, and the sources of these funds must be documented. Geriatric Mental Health Academic awardees may not be required, as a condition of institutional supplementation, to perform additional duties which prolong or detract from the program.

In addition to the base salary, the institution's share of contributions to finance such fringe benefits as are available to all other faculty and staff of comparable rank and seniority at the institution, under formally established and consistently applied institutional policies, may be paid from award funds to the extent they are consistently treated by the institution as direct rather than indirect costs. An annual support allowance of up to $5,000 may be requested for part-time secretarial support, supplies, study at centers other than the sponsoring institution, tuition or fees for such study, and travel and per diem allowance for participation in a professional meeting. Relocation expenses from place of residence to the applicant institution are not allowable. An annual research allowance of up to $5,000 may be requested for support of research activities, pilot studies, or instrumentation development. Details and justification of both support allowance and research allowance requests must be provided in the budget section of the application. All grants will receive indirect costs at a rate of 8 percent of total allowable direct costs or at the actual indirect cost rate, whichever is less. Indirect costs are not provided for tuition and related fees and expenditures for equipment. Awards will be governed by the "PHS Grants Policy Statement."

A Geriatric Mental Health Academic Award application may not be submitted concurrently with an application for a Research Scientist Development Award, Faculty Development Award, an individual National Research Service Award, or other career-development type award of ADAMHA or NIH. Nor may the Academic Award be held concurrently with any of the above awards.

APPLICATION REQUIREMENTS

The applicant should use the following outline to prepare Sections A through D of the Research Plan Section of the application:

I. Description of the Nominee and Applicant Institution Characteristics at the Time of Application

   A. Geriatric Mental Health Academic Award Nominee - The nominee should provide a self-assessment, indicating areas of strength and weakness in geriatric research and clinical experience and details of the nominee's goals during the period of award. The nominee should be listed as the Principal Investigator/Program Director for the application.

   B. Supervisor - Supervision of the nominee during the award will be the responsibility (directly or delegated with oversight) of the head of the applicant professional school (e.g., Dean, Department Chairperson, etc.). A description of the role he/she will play in relation to the major activities of the Geriatric Mental Health Academic Award nominee throughout the award period should be included. If supervision is to be delegated to another faculty person or sponsor, this individual's role and the relation this individual has to the head of the applicant professional school should be described.

C. Experts - If neither the supervisor nor the delegated faculty has suitable proficiency in research methodology and clinical geriatrics, experts in these areas must be identified, and letters of agreement to consult with the nominee and supervisor must be provided. The role of each expert should be identified; the nature of the relationship between expert, supervisor, and nominee should be described; and the financial or other arrangements should be detailed.

NOTE: The Biographical Sketch form provided in the application kit (PHS Form 398) should be completed so that it provides a complete curriculum vitae of the Geriatric Mental Health Academic Award nominee. Biographic sketches for the supervisor and for each expert identified (C., above) should also be included in the application.

D. Applicant Institution - The applicant is expected to demonstrate the need for a specially prepared faculty member to implement a research and education program in geriatric mental health in the professional school; i.e., the applicant must demonstrate that, while there is a commitment to establishing the geriatric mental health research program, current faculty resources do not permit the establishment of such a program. Although priority will be given to those applicants who propose to establish a geriatric mental health program in an institution, some consideration will be given to applicants proposing expansion of a program beyond a limited base presently available in the institution. It is the joint responsibility of both supervisor and nominee to provide general information about the applicant institution, including history, size, and educational philosophy of the sponsoring department or school, and to describe the current curriculum and research activities in mental health of the aging.

II. Plans and Activities

A. Geriatric Mental Health Academic Award Nominee - The nominee should develop a 3-year plan for activities which will result in his/her ability to fulfill the responsibilities involved in this award: researcher, developer of other researchers, and consultation resource in research and clinical settings within the institutional program. The plan should include description of areas where additional preparation will be required and the activities projected to develop competence in these areas. Specific content areas within geriatric mental health and the methodological approaches on which the nominee will focus should also be described. A plan for each year of the award should be presented. The candidate is expected to devote full time to the proposed research and academic development activities. The activities might include collaboration in research projects, development of pilot studies, participation in structured academic courses, tutorial arrangements, consultation with geriatric mental health experts, independent study and supervised clinical experience. Although apportionment of time among activities will be based on the nominee's needs, the total program must be well balanced, and activities to enhance geriatric mental health research expertise must constitute the major part of the awardee's activities. Approximate distribution of time among categories of activity should be provided. The program may require a period of study specifically on research in mental health of the aging at another institution. Sites of anticipated activity should be identified; financial arrangements between the applicant institution and any other sites should be described, e.g., tutorial services or tuition and fees paid by the applicant institution to the site.

B. Institutional Plans - The applicant institution must assure that the Geriatric Mental Health Academic Award nominee will be released from activities not directly related to his/her development as an academic researcher and resource in geriatric mental health. The nominee may continue to be involved in activities within the school which are appropriate to the accomplishment of the program goals. Thus, the nominee's responsibilities may include, in addition to pursuit of a professional development activity on research projects, development of curricula in geriatric mental health, teaching and/or coordination of educational or clinical activities in geriatric mental health, and provision of consultation to faculty colleagues and community groups. The application should describe the resources of the institution which are or will be committed to the advancement of the nominee and geriatric mental health as a component of its total academic research and teaching program, both during and subsequent to the award.

III. Plans for Post-Award Activities

The nominee and the head of the sponsoring department should describe the long-term goals of the school or department in geriatric mental health research and teaching. How the Geriatric Mental Health Academic Award will help achieve these goals should be discussed.

IV. Evaluation Activities

Each application should include a description of procedures by which progress of the nominee in the program and impact of the program on the institution will be measured and evaluated, along with a description of how the findings from continuous evaluation will be fed back into the program. The evaluation data will be used by NIMH in assessing the strength of the program. Such data could include the amount and types of material and the time devoted to geriatric issues in instructional programs, the type and number of collaborative arrangements for research or teaching between the academic program and treatment or service settings for the elderly, and research projects proposed or developed in geriatric mental health.

APPLICATION AND REVIEW PROCEDURES AND CRITERIA

Applications - All applicants should use form PHS 398 (Rev. 5/80). Application kits are available in university grants offices or from the following office:

Grants Operations Section
National Institutes of Mental Health
Parklawn Building Room 7C-05
5600 Fishers Lane
Rockville, Maryland 20857

Instructions for applicants are included in the kit.

The signed original and six (6) copies should be sent directly to the following address:

Division of Research Grants
National Institutes of Health
Westwood Building
5333 Westbard Avenue
Bethesda, Maryland 20205

Grant Review Procedures - Research grant applications are reviewed for scientific and technical merit by an initial review group (IRG), composed primarily of non-Federal scientific experts, and by the National Advisory Mental Health Council. By law, only projects recommended for approval by the Council may be considered for funding. Summaries of IRG recommendations are sent to applicants as soon as possible after the Council has completed its review.

Review Schedule - NIMH research grant applications are reviewed according to the following schedule:

Review Schedule

Receipt Dates	Initial Review Group Meetings	National Advisory Mental Health Council Meetings	Approximate Start Date
July 1	Oct. - Nov.	Jan. - Feb.	April 1
Nov. 1	Feb. - March	May	July 1
March 1	June	Sept. - Oct.	Dec. 1

Review Criteria - In the review of Geriatric Mental Health Academic Award applications, Initial Review Groups consider the background and potential of an individual nominee as an investigator, a teacher of other investigators, and a resource in the research, educational, and clinical programs of the institution. In addition, the Initial Review Groups consider the quality and feasibility of the development plan, the merit of the institutional plan and commitment presented, and the quality of the institutional plan to incorporate a strong geriatric mental health component in its research and teaching programs.

Council review also involves questions of policy and program priorities.

Staff Consultation - Potential applicants may seek information and consultation from the staff of the following:

Center for Studies of the Mental Health
of the Aging
National Institute of Mental Health
Parklawn Building - Room 11A16
5600 Fishers Lane
Rockville, Maryland 20857

Telephone: (301)-443-1185

Inquiries should be directed to:

Gene D. Cohen, M.D., Ph.D., Chief
or
Barry D. Lebowitz, Ph.D., Head
Research Program

Award Criteria - Initial Review Group and Council recommendations, significance of the particular topical approach, program balance, priorities indicated elsewhere in this announcement, and availability of funds are taken into consideration in determining which projects will be funded.

Period of Support - The Geriatric Mental Health Academic Award is made on an annual basis, with additional years of recommended support for a total of up to 3 years. It is not renewable. Support for the second and third year of the award is contingent upon receipt of an application annually which provides a summary report of progress to date, plans for the next year, and appraisal of the awardee's progress submitted by the sponsor. Continuation applications are due 60 days before the termination of the current budget period; application forms will be sent to the awardee.

ANNOUNCEMENT

RESEARCH INTERESTS IN EPIDERMOLYSIS BULLOSA, SKIN DISEASES PROGRAM

NATIONAL INSTITUTE OF ARTHRITIS, DIABETES, AND DIGESTIVE AND KIDNEY DISEASES

The Skin Diseases Program of the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases is encouraging the submission of applications for research grants in epidermolysis bullosa (EB), a group of inherited skin disorders characterized by the formation of blisters and erosions at the site of mild trauma. In the less severe form, EB simplex, blisters are usually confined to the hands and feet. The more severe recessive dystrophic form may involve the entire body, and is associated with even greater morbidity and significant mortality. Repeated blistering causes infection, malnutrition, flexural contractures, and mitten-like deformities of the hand and feet.

Although the cause of EB is unknown, there is some evidence that in recessive EB there is degeneration and phagocytosis of collagen fibrils in the area of blistering. Increased collagenase activity in organ cultures of blistered skin has recently been demonstrated.

The NIADDK seeks studies aimed at achieving a better understanding of pathophysiologic mechanisms which contribute to the onset of EB as well as further insight into the process of epidermal cleavage in general. Proposals utilizing research advances in genetics, pathology, cell biology, biochemistry, and immunology as they pertain to various types of EB and the blistering process are encouraged.

The Skin Diseases Program also encourages the submission of applications for research training through National Research Service Awards, both individual fellowships and institutional awards; Clinical Investigator Awards, New Investigator Research Awards, and Research Career Development Awards.

METHOD AND CRITERIA OF REVIEW

Assignment of Applications - Applications will be received by the NIH's Division of Research Grants, referred to an appropriate initial review group for scientific review, and assigned to the NIADDK for possible funding. These decisions will be governed by programmatic considerations as specified in the DRG Referral Guidelines.

This program is described in the Catalog of Federal Domestic Assistance No. 13.846, Arthritis, Bone, & Skin Diseases. Awards will be made under the authority of the Public Health Service Acts, Sections 301 (Public Law 78-410, as amended; 42 USC 241) and 472 (42 USC 2891-1) and administered under PHS grants policies and Federal Regulation 42 CFR Parts 52 and 66 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

Review Procedures - Applications in response to this announcement will be reviewed in accordance with the National Institutes of Health peer review procedures. They will first be reviewed for scientific and technical merit by a review group composed mostly of non-Federal scientific consultants. Following initial review, the application will be evaluated for program relevance by the NADDK Advisory Council. Review criteria customarily employed by the National Institutes of Health for regular research grant applications will prevail. Approved applications will compete for available funds with other approved grant applications assigned to the NIADDK.

Deadline - Applications will be accepted in accordance with the announced receipt dates for new applications (see receipt dates and review schedule in Application kits).

Method of Applying - Applications for research grants should be submitted on form PHS 398, which is available in the business or grants and contracts office at most academic and research institutions or from the Division of Research Grants, NIH. The phrase "PREPARED IN RESPONSE TO RESEARCH GRANTS ANNOUNCEMENT IN THE AREA OF EPIDERMOLYSIS BULLOSA" should be typed across the top of the first page of the application.

The original and six copies of the application should be sent or delivered to:

Application Receipt Office
Division of Research Grants
National Institutes of Health
Westwood Building Room 240
Bethesda, Maryland 20205

For further information or to obtain application kits, investigators are encouraged to contact the program director:

Alan N. Moshell, M.D.
Skin Diseases Program Director
National Institute of Arthritis, Diabetes,
and Digestive and Kidney Diseases
National Institutes of Health
Westwood Building Room 405
Bethesda, Maryland 20205

Telephone: (301) 496-7326

ANNOUNCEMENT

ADOLESCENCE RESEARCH

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

I. BACKGROUND

The National Institute of Child Health and Human Development (NICHD) supports and conducts research to improve the health and well-being of the developing infant and child and to prevent conditions that have their origins early in life and may lead to adult disabilities and early death. The events of pregnancy (especially during adolescence), labor, and birth present some of the greatest opportunities for intervention that can prevent many of these disabilities. Adolescence is also a time in human development when profound physical and behavioral changes are taking place. The NICHD, therefore, has a major interest in supporting fundamental research related to biomedical and behavioral aspects of adolescence. The Institute provides this support through two extramural research centers: the Center for Research for Mothers and Children and the Center for Population Research.

II. CENTER FOR RESEARCH FOR MOTHERS AND CHILDREN: RESEARCH GOALS AND SCOPE

The Center for Research for Mothers and Children (CRMC) through two of its extramural branches, supports research concerning adolescence:

The Clinical Nutrition and Early Development Branch (CNED) is concerned with the special nutritional requirements of the adolescent and those factors related to food choice and obesity. The CNED is also concerned with pregnancy during adolescence, particularly in those under sixteen years.

The Human Learning and Behavior Branch (HLB) is concerned with the biobehavioral, cognitive, social and affective development of normal adolescents and those factors which may interfere with normal development.

This program is supported under Title III, Section 301 and Title IV, Section 441 (Public Law 78-410, as amended: 42 USC 241). The Catalog of Federal Domestic Assistance numbers are 18.865, Research for Mothers and Children and 13.864, Population Research. Awards will be administered under PHS Grant Policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. These programs are not subject to A-95 Clearinghouse or Health Systems Agency review.

The National Institute of Child Health and Human Development (NICHD) and the National Institute of Mental Health (NIMH) are announcing their interest in supporting research on adolescence. Accepted referral guidelines will be followed in assigning applications. Although the missions of these Institutes are different, some research projects could appropriately receive support from either organization. Dual assignment of such applications is intended to assure that projects of the highest quality are able to be supported.

A. Adolescent Nutrition

Adolescence is a time of profound transformation. Growth rates are exceeded only by those occurring during fetal life and early infancy. Assessment of nutritional status is particularly difficult during this period with food patterns often erratic. The following represent some research areas of special interest to NICHD:

1. Definition of nutrient requirements associated with the adolescent growth spurt and the onset of puberty.

2. Development of new methods and validation of existing methods for assessing nutritional status that are particularly applicable to adolescence.

3. Elucidation of the cognitive, emotional, and social processes involved in food choices by adolescents. Attention needs to be focused on the regulation of food intake and the effect of external environmental cues on eating behavior.

4. Investigation of exercise and energy balance as these contribute to the development of obesity during adolescence as well as studies of potential and undesirable health effects of weight reduction regimens on the obese young adolescent still undergoing physiologic maturation.

5. Exploration of the psychological and cultural determinants of adolescent obesity. Studies are encouraged leading to techniques for modifying eating behavior and stimulating obese adolescents to lead more active, healthful life styles.

B. Adolescent Pregnancy

Pregnancy during adolescence, particularly in those under sixteen years of age, impose additional stress on a young woman still undergoing maturation. The following require research attention:

1. Investigation of short-term and long-term biomedical sequaiae in the mother of uncomplicated pregnancy in early adolescence.

2. Identification of quantifiable indicators of adolescent maternal and fetal health at various times during pregnancy in order to improve prenatal care, particularly in the highest risk populations.

3. Definition of energy and nutrient demands of lactation superimposed on the growth process in the young adolescent mother in terms of health and development of both mother and child.

4. Exploration of physiologic and metabolic differences between pregnancy as well as non-pregnant young adolescents and older gravidas, including the disposition and action of pharmacologic agents such as ethanol and nicotine, as well as other agents used therapeutically.

For further information about the research support activities related to adolescent nutrition and pregnancy you may contact:

Dr. Merrill S. Read, Chief
Clinical Nutrition and Early Development Branch
Center for Research for Mothers and Children
National Institute of Child Health
and Human Development
National Institutes of Health
Bethesda, Maryland 20205
(301) 496-5575

C. Adolescent Biobehavioral Development

The following areas of research are of major interest:

1. The relationships between alterations in hormone levels and behavioral development during adolescence. Development variables may include gender-role identity, mood, patterns of peer and social interaction and cognition.

2. Electrophysiological studies of brain development during adolescence in relation to cognition, maturation of language and perception. Of particular interest are studies of brain laterality and the normative development of cognition, thinking, memory, perception, and learning.

3. Studies of the effects of rapid changes in physical growth (height, weight, secondary sexual characteristics, muscular development and coordination, etc.) on the development of self-concept in adolescent boys and girls. Of particular interest is the role played by menarche in adolescent females in their development of self-concept and gender-role.

D. Adolescent Cognitive Development

The following areas of research are of major interest:

1. Changes in cognitive style.
2. Changes in thinking styles.
3. Changes in language ability.
4. Changes in reasoning ability.
5. Changes in memory capacity.

E. Adolescent Social and Affective Development

The following areas of research are of major interest:

1. Changes in relationships within the family (parents, siblings), and outside the family, including other adults and peers.

2. Personality development including changes in the adolescent's concept of self from that of immaturity and dependence to a sense of competence, self-regard, autonomy, and the assumption of adult roles (including work and career orientations).

3. Differences related to sex-role behavior and identity, reflecting differing adolescent experiences and expectations between males and females.

4. The nature of the adolescent period, the critical events during that period, and the development of competency in handling such events.

5. Antecedent conditions that lead to risk-taking behaviors.

6. Antecedent conditions that lead to prosocial behaviors, e.g., affiliation, nurturance, generosity, and sharing.

For further information about the research support activities described above you may contact:

Dr. Norman Krasnegor, Chief
Human Learning and Behavior Branch
Center for Research for Mothers and Children
National Institute of Child Health
and Human Development
National Institutes of Health
Bethesda, Maryland 20205

Telephone: (301) 496-6591

III. CENTER FOR POPULATION RESEARCH: RESEARCH GOALS AND SCOPE

The Center for Population Research has a long-standing and continuing interest in the demographic, psychological, economic, social, and other antecedents and consequences of fertility. The Center has funded research in such areas as fertility regulation and family planning, fertility trends, childbearing patterns, female employment and fertility, adolescent pregnancy and fertility, and consequences of family size.

The Social and Behavioral Sciences Branch of the Center for Population Research is calling attention to a number of important fields in which there has been relatively little research. The areas thus targeted as in need of research include:

A. Antecedents of Risking Unintended Pregnancies

B. Consequences of Pregnancy Losses for Adolescents

C. Adolescent Childbearing and the Family

D. Prevention of Adolescent Pregnancy

The following program announcements have the purpose of encouraging the submission of research grant applications in these designated research areas.

A. Antecedents of Risking Unintended Pregnancies

Even though the use of methods of fertility regulation has increased, the incidence of unprotected intercourse remains fairly high. A large number of unintended pregnancies, especially among adolescents, continues to occur. Numerous investigators have attempted to discover the factors involved in unintended pregnancies. However, available data on the reasons for unintended pregnancies are fragmentary, few in-depth studies have been conducted, and some important segments of the population have received relatively little attention.

Studies in this area tend to be descriptive and unsystematic, rather than based on comprehensive theoretical and conceptual frameworks, substantiated by empirical evidence. Research is needed that focuses on the antecedents of unprotected sexual relations, thereby elucidating the factors associated with and contributing to the non-use or infrequent use of fertility regulating methods. In developing research design and methodology, attention should be given to why past studies may not have produced sufficiently definitive results.

What are the relative strengths of biological demographic, psychological, social cultural, economic, and other factors that interact as antecedents of the unprotected sexual relations of married and unmarried males and females? Examples of such factors include age, sex, ethnicity, race, educational attainments, occupation, marital status, socioeconomic status, biological development, psychological characteristics (developmental level, maturity, personality, attitudes, motivations, planfulness, etc.), personal/social relationships (with partners, parents, peers, etc.), knowledge of and attitudes toward sex and reproduction, knowledge of and attitudes toward fertility regulating methods and service providers (physicians, clinic staffs, etc.), pregnancy and abortion history, living situations and conditions, and life events.

It may be beneficial to the research to include a conceptual model based on theories in such relevant areas as motivation, decision-making, risk-taking, and cognition. In-depth approaches and innovative designs may contribute to the empirical testing of such a conceptual model focusing on unprotected sexual relations.

Care should be taken to develop efficient and cost-effective research designs. Familiarity with the literature on the antecedents of unprotected sexual relations, including relevant theories and empirical studies, should be demonstrated.

One objective of the research should be to develop findings and test theories and implications for the prevention of unintended pregnancies. Both scientific understanding and practical application may be advanced by approaches that would attempt to develop group and individual profiles of persons with high probability of (a) risking unintended pregnancies, (b) abstaining from sexual relations, or (c) using effective contraception.

B. Consequences of Pregnancy Losses for Adolescents

Adolescents experience about 500,000 pregnancy losses per year, of which approximately 400,000 are induced abortions, and about 100,000 are miscarriages. Considerable research has been done on the consequences of abortion for women who are beyond adolescence. However, there is a paucity of research on the psychological, social, health, and other consequences of abortions for adolescents, and there is practically no research on the consequences of miscarriages for adolescents. In-depth research on these problems is needed because important differences between adolescents and adults may contribute significantly to differential consequences of pregnancy losses. For example, adults and adolescents differ in biological, psychological, social, and educational maturity. Also there are differences in such factors as life-style and degree of independence, as well as in relationships with parents, other family members, sexual partners, peers, friends, and service providers.

How do various relevant factors interact to contribute to the psychological, social, health and other consequences of pregnancy losses for adolescents, including subsequent sexual and fertility regulating behavior. Factors which may be considered include age, race, ethnicity, educational status, level of development and maturity (biological, psychological, social), personal/social relationships (with parents, partners, peers, etc.), service providers (physicians, clinic staffs, etc.), religion, socioeconomic status, pregnancy and abortion history, use of fertility regulating methods, length of time following abortions and or miscarriages, and life events following abortions and/or miscarriages, and life events following abortions and/or miscarriages (living with parents, marriage, dropping out of school, obtaining employment, etc.). The effect of the pregnancy loss on the male partner is also of interest.

The identification of appropriate comparison groups for adolescents who obtain abortions or have miscarriages is a major problem of the research design, which requires special consideration and innovative approaches. The research design should include a conceptual model of the interrelationships among factors assumed to affect the consequences of pregnancy losses for adolescents. Careful selection of variables and samples within a well-defined conceptual framework should contribute to the development of efficient and cost-effective designs.

An understanding of the consequences of pregnancy losses should provide adolescents with better bases for making decisions about engaging in sexual relations, using contraception, and resolving unintended pregnancies. Such knowledge and understanding should also be of value to parents, counselors, physicians, teachers, and others who make important contributions to adolescent decision-making.

C. Adolescent Childbearing and the Family

Considerable research has addressed the effects of early childbearing on the young mothers involved and on their offspring. However, less attention has been paid to the effects on young fathers and the extended families involved. Similarly, research on the antecedents of early sexual, contraceptive, and fertility-related behavior has focused largely on the characteristics of the young woman, less on the male or the partner relationship, and least on the role of the adolescents' families. This announcement focuses on the role of the adolescents' family in influencing fertility-related behavior and the effects of that behavior on the family. Current research suggests that the families of adolescent parents, especially unmarried mothers, are heavily involved in the consequences of her birth. The grandmother may become a major care-giver for the baby, and the family may provide room and board or direct financial support. It appears that family involvement is beneficial for the adolescent mother, often enabling her to return to school, a key to future economic well-being. Also children of adolescent mothers appear to benefit from the involvement of another adult, especially an experienced care-giver. There is, however, no comprehensive picture of the social, economic, emotional and other effects of adolescent childbearing on the family. Is the grandmother likely to drop out of the labor force to care for the infant or is she likely to enter the labor force to help defray additional costs? Are there economic impacts for other family members? Does the parental family benefit from the experience of helping to rear the adolescent's baby or does such involvement introduce special strains into the grandparents' marital relationship, the parent-child relationships, or relationships among siblings? There is also interest in research on the role of the family as an antecedent of adolescent sexual and fertility-related behaviors. The likelihood of an adolescent engaging in sexual relationships appears to depend, in part, on family structure, religion, socioeconomic status, educational aspirations and other factors heavily influenced by the attitudes, values and behaviors of parents.

The research design should include a conceptual model of the interrelationships among factors associated with adolescent behavior and the role of the family. Careful selection of variables and samples within a well-defined conceptual framework should contribute to the development of efficient and cost-effective designs.

D. Prevention of Adolescent Pregnancy

There are approximately a million teenage pregnancies a year, of which about seventy-five percent are unintended. There are indications that these figures will increase unless ways are found to prevent the pregnancies. A major determinant of future trends is the continuing increase of sexual activity among unmarried adolescents with the majority of these sexually active teenagers either never practicing contraception or practicing it inconsistently.

Basic, non-operational research is needed to develop theories and evidence upon which attempts to prevent adolescent pregnancies may be based. A major aim of such research is the development of theory and data bases regarding the malleability of behavior in these areas. While much can be done in the area of teen fertility regarding program evaluation, that is not the goal of this announcement. The goal here is to support basic research on the factors associated with adolescent pregnancies, the likelihood that behavior can be modified, and the circumstances under which it can be changed.

Hypotheses concerning the modification of adolescent fertility-related behavior could be tested in research with clear and direct implications for initiating or developing practicable, feasible and balanced approaches to preventing adolescent pregnancies. The formulation of hypotheses could be based on analyses of the literature concerning determinants and consequences of adolescent pregnancies. However, fruitful leads may also be discovered by analyzing selected literature on relevant aspects of adolescent development and behavior.

What are the characteristics and behavior of adolescents to which attention should be given when attempting to develop theories and findings upon which approaches to the prevention of pregnancy might be based? Examples of such characteristics and behavior include developmental level (biological, psychological, social, etc.), age, sex, race/ethnicity, socioeconomic status, education, religion, motivation, attitudes, personality, emotion, values, morals, knowledge, learning and congnitive skills, and decision-making.

What are the life experiences, situations, or activities that may influence adolescent behavior and characteristics toward the prevention of pregnancies? Examples include educational activities (sex, health, parental, and other kinds of education), socialization processes (peer, family, community, etc.), counseling (individual, group, etc.), contraceptive practices, kinds and accessibility of service-providers, religion, and couple relationships.

Investigators may study the role of one or two factors in the prevention of pregnancy. However, since pregnancy prevention is a multifaceted problem, investigators may also study the implications of a number of interacting factors for feasible pregnancy prevention activities. Investigators may use interdisciplinary or disciplinary approaches to the problems of pregnancy prevention.

There is need for ingenious and innovative research designs that will make it possible to compare and evaluate the roles which one or more factors may play in the prevention of pregnancy. Innovative designs may be able to accomplish the objectives with relatively small-scale studies in which there has been careful selection of variables and study participants with a well-developed conceptual framework. Investigators may be able to locate existing situations which can be subjected to meaningful, comparative analyses. These suggestions are not intended to limit research designs or the scale of the studies, but to request that careful attention be paid to developing efficient, cost-effective designs. Research must be planned with the aim of developing theories and findings with implications for feasible, workable approaches to preventing pregnancy.

Correspondence, including request for advice on further development of applications in any of the areas targeted by the Center for Population Research as needing research, should be directed to:

Dr. Sidney H. Newman
Social and Behavioral Sciences Branch
Center for Population Research
National Institute of Child Health
  and Human Development
Landow Building, Room 7C25
7910 Woodmont Avenue
Bethesda, Maryland 20205

Telephone: (301) 496-1174

IV. MECHANISMS OF SUPPORT

A variety of mechanisms are available for obtaining grant support under this program:

1. The research project grant, the traditional NICHD research support mechanism;

2. The New Investigator Research Award, a mechanism described in the NIH Guide for Grants and Contracts Volume 9, No. 1, January 3, 1980; and

3. The program project grant, a mechanism available for multidisciplinary research involving at least three projects with a common focus.

V. CRITERIA FOR REVIEW

Applications compete on the basis of relative scientific merit with all grant applications before the NICHD. They are formally reviewed by NIH peer review groups and by the NICHD National Advisory Council. The number of awards made will reflect both relative merit and the availability of grant funds. Some applications reflect overlapping interests of more than one Institute for funding purposes. The criteria for review are the traditional considerations underlying scientific merit which include adequacy and appropriateness of the approach; training, experience, and research competence or promise of the investigator(s); the adequacy of the research design; the suitability of the facility; and the appropriateness of the requested budget relative to the work proposed.

VI. METHOD OF APPLYING

Applicants are asked to notify the NICHD representative at least one month prior to formal submission of an application. Include name of principal investigator, institutional address, title of application, and abstract of the proposed research. Indicate that the application is in response to this announcement.

For research projects and New Investigator Research Awards, use form PHS 398 (Revised 5/80). If your institution does not have these, copies may be obtained from:

Office of Grants Inquiries
Division of Research Grants
National Institutes of Health
Bethesda, Maryland 20205

Telephone: (301) 496-7441

Information concerning program project grants and how to apply can be obtained from SBSB staff.

After you have completed the application, expedite its routing within NIH by:

1. Checking the box, item 2, on the application form indicating that your proposal is in response to this announcement: NICHD ADOLESCENCE RESEARCH. Indicate also the Center and the topic to which the application is addressed.

2. Attaching a cover letter repeating that this application is in response to the announcement: NICHD ADOLESCENCE RESEARCH.

Forward application and cover letter to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205

Receipt dates for research project grants and New Investigator Research Award applications are: July 1, November 1, and March 1; receipt dates for the program project grant: June 1, October 1, and February 1.

ANNOUNCEMENT

RESEARCH ON STRESS REACTIVITY IN ADOLESCENCE

NATIONAL INSTITUTE OF MENTAL HEALTH (ALCOHOL, DRUG ABUSE, AND MENTAL HEALTH ADMINISTRATION, PUBLIC HEALTH SERVICE)

Subject to availability of funds, applications for mental health research grants will be accepted by NIMH under receipt dates indicated herein.

I. PURPOSE

This is a request for research grant applications to increase our knowledge of the mechanisms and conditions of stress reactivity in adolescence.

Research on both adolescence and stress is part of a continuing concern of the National Institute of Mental Health. However, we need to specify the mechanisms and conditions of stress reactivity in adolescence that influence mental health or illness. The goal of the National Institute of Mental Health in issuing this announcement is to encourage basic and applied adaptational coping in adolescence.

II. BACKGROUND

Adolescence is the only age group in the country in which the death rate is rising. Improved health measures have prolonged the life of the elderly and have increased survival in early childhood, but teenagers are dying in increasing numbers due to suicide, homicide, drug abuse, and alcohol-related automobile accidents. High rates of teenage pregnancy and juvenile crime are problems acknowledged by society while many parents are concerned about the prolonged and painful transition of their own children into adult roles.

Many of these problems are the concerns of agencies other than the National Institute of Mental Health. Our specific interest is in the stress and turmoil which may be implicated in the etiology of mental, emotional and behavioral disorders.*

Under authority of Section 301 of the Public Health Service Act, as amended, P.L. 78-410, 42 U.S.C. 241 (42 CFR Part 52), the National Institute of Mental Health (NIMH) is accepting applications for research grants for the support of research on stress reactivity in adolescence. This program is described in the Catalog of Federal Domestic Assistance No. 13.242, Mental Health Research, and administered under PHS grant policies and Federal regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

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* The National Institute of Child Health and Human Development (NICHD) and the National Institute of Mental Health (NIMH) are announcing their interest in supporting research on adolescence. Accepted referral guidelines will be followed in assigning applications. Although the missions of these Institutes are different, some research projects could appropriately receive support from either organization. Dual assignment of such applications is intended to assure that projects of the highest quality are able to be supported.

While the past portrayal of adolescence carried too heavy an emphasis on turmoil and maladaption, current studies support a more benign view of "normative crisis" in which the adolescent process is seen as difficult but normal. This is not to say that all adolescents have a difficult time. But many do because adolescence is a period of extraordinary change, multiple conflicts, and marked societal demands upon the individual.

On the side of change, there are the hormonal, physiologic, and somatic changes reflected in pubertal development. Equally important psychological changes are spurred on by this rapid physical development, or perhaps occur concomitantly and interact with it. Cognitive changes during this period, including formal logic, may account for some of the shifts that take place. Among the psychosocial demands induced by puberty are: a heightened sexuality, the growth of peer attachments, a striving to achieve autonomy from and to reduce dependency on parents, the assumption of specific gender roles, and a heightened search for personal identity.

These multiple changes can be viewed as stressors in the sense that they entail significant adaptation needed to restore a sense of homeostasis to the individual.

III. SPECIFIC AREAS OF INTEREST

In order to improve our ability to understand, treat, and prevent mental, emotional, and behavioral disorders, we are interested in increasing our knowledge about stress from a developmental perspective. There are complex interactions that occur among biological, cognitive, affective, and behavioral aspects within the individual as well as between any of these aspects and features of the external environment. Furthermore, this process involves reciprocal influences between aspects. Proposals may involve interdisciplinary research approaches between biological, cognitive, affective, and behavioral aspects of stress, as well as between any of these aspects and the environment.

The timing of developmental changes, the extent of preparation for the changes, individual vulnerability, and social supports all serve to mediate the effects of developmental stress in adolescence. These same mediators operate not only with normative developmental stressors but with unpredictable stressors as well.

The developmental tasks of adolescence can be associated with normative stresses that have intrapsychic or environmental origins. The stressors trigger a range of responses that vary from adaptive to maladaptive. The responses can be mediated by psychosocial and/or physiological mechanisms. What are the relationships between the normative stressors of adolescence, coping mechanisms, and adaptive and maladaptive responses? How are defense mechanisms utilized to effectively channel intense affects? How are disruptive arousal states avoided? What are the factors that lead to the failure of defensive operations?

Many researchable issues fall within the realm of stress reactivity in adolescence. It should especially be noted that in speaking of stress reactivity, we are speaking of functional as well as dysfunctional reactions to stress and we would like to know how some adolescents cope in spite of great obstacles or handicaps.

The following are offered as illustrations of appropriate topics, but applications need not be limited to these issues:

Biological Development

Puberty involves dramatic internal endocrine changes as well as dramatic external physical changes. What are the important psychological changes spurred by this development and how do they affect stress reactivity? How are such stresses mediated? What are characteristic relationships between stressors, physiological mechanisms, and maladaptive behavior? How can neuroendocrine responses to stress facilitate adaptation in adolescence?

Cognitive Development

Young people develop the capacity to think about thinking during the adolescent years. Does cognitive change amplify the stress of adolescence or does it facilitate coping?

Peer Relations

What are the functions and costs of peer conformity in relationship to normative stresses during adolescence?

Parents

Relationships with parents change during adolescence. The transition in the nature of the adolescent/parent relationship may proceed smoothly or it may be very difficult. Under what circumstances do the changes of this period create stress and under what circumstances do parental relationships help modulate stress?

Preparation for Change

The extent of preparation for the changes of adolescence tends to mediate the effects of developmental stress. The adolescent must observe situational cues; understand the meaning of situational demands in relation to individual, familial, peer, and societal values; define and select from alternative plans of action; and finally to consummate plans. What developmental limitations increase the stress of negotiating these tasks?

In addition to the above substantive topics, methodological projects which promise new understanding of the complex processes which influence adolescent stress reactivity will be considered. The employment of pre-existing data sets and their secondary analysis is encouraged provided they meet all the criteria of scientific merit.

IV. ELIGIBILITY REQUIREMENTS

Grants may be made to public or private nonprofit or for-profit institutions, organizations, qualified Federal entities, state or local governments and their agencies.

V. FUNDING AND TERMS AND CONDITIONS OF SUPPORT

Funds estimated at one million dollars per year are available to support applications submitted in response to this announcement.

Grants are awarded directly to the applicant institution. Grant funds may be used only for those expenses which are directly related to and necessary to carry out the research project, and must be expended in conformance with DHHS cost principles, the Public Health Service Grants Policy Statement, applicable Federal regulations, and conditions set forth in the grant award document. In general, grant funds may be used for: (1) direct costs which are necessary to carry out the project, including salaries, consultant fees, supplies and equipment, and essential travel; and (2) actual indirect costs to cover related overhead. The maximum initial period of grant support will, in general, be limited to three years. Applications will undergo full review and compete for available funds with other approved projects.

VI. APPLICATION PROCEDURES

Applicants should use form PHS 398 (Rev. 5/80). State and local government agencies should use form PHS 5161. Form PHS 398 can ordinarily be obtained from the Office of Sponsored Programs of a university. Both application kits are also available from the following:

Grants Operations Section
Grants Management Branch
National Institute of Mental Health
Parklawn Building Room 7C-05
5600 Fishers Lane
Rociville, Maryland 20857

Telephone: (301) 443-4414

Instructions for applicants are included in the kit. The phrase, "STRESS REACTIVITY IN ADOLESCENCE" should be entered in item 2 on the face page of the application.

The signed original and six copies of the application should be sent directly to the following:

Division of Research Grants
National Institutes of Health
Bethesda, Maryland 20205

VII. CONTACT OFFICE

Investigators considering submitting an application in response to this program announcement are strongly encouraged to discuss their project with NIMH staff in advance of formal submission. This can be done either through a telephone conversation or through a written and brief (4-5 pages) research prospectus. For further information, investigators are encouraged to contact:

Sigmund E. Dragastin, Ph.D.
Chief, Personality and Emotional Processes
and Problems Section
Behavioral Sciences Research Branch
National Institutes of Mental Health
Parklawn Building Room 10C-09
5600 Fishers Lane
Rockville, Maryland 20857

Telephone: (301) 443-3942

VIII. RECEIPT AND REVIEW SCHEDULE

Applications will be accepted under an initial receipt date of July 1, 1982. Applications received by that date will receive initial scientific review in October-November 1982, and review by the National Advisory Mental Health Council in February 1983, with possible funding by April 1983. The initial and subsequent receipt dates are:

Receipt Date	Initial Review	Council Review	Earliest Award Date
July 1	Oct. - Nov.	February	April
November 1	Feb. - March	May	July
March 1	June	September	November

IX. REVIEW PROCEDURES AND CRITERIA

Applications submitted in response to this announcement will be reviewed in accordance with the usual Public Health Service peer review procedures for research grants. They will be reviewed first for scientific and technical merit by a review group composed primarily of non-Federal scientific consultants (Initial Review Group) and then by the National Advisory Mental Health Council. Only those applications recommended for approval by Council will be considered for funding.

Factors considered in evaluating applications include, but are not limited to:

- Scientific and technical merit of the research design, approach, and methodology.
- Originality and appropriateness of the conceptualization of the research.
- Potential contribution of the research to the field.
- Qualifications and experiences of the principal investigator and proposed staff.
- Availability of resources necessary to the research.
- Reasonableness of the proposed budget in terms of the research proposal.

X. AWARD CRITERIA

Award decisions will be based on scientific merit as judged by initial review committee and Council and on the potential of the research for contributing to our understanding of the etiology, treatment or prevention of mental and behavioral disorders.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

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HAVE YOU MOVED?

If your present address differs from that shown on the address label, please send your new address to: Grants and Contract Guide Distribution Center, National Institutes of Health, Room B3BN10, Building 31, Bethesda, Maryland 20205, and attach your address label to your letter. Prompt notice of your change of address will prevent your name from being removed from our mailing list.

The GUIDE is published at irregular intervals to announce scientific initiatives and to provide policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in grants and contracts activities administered by the National Institutes of Health.

Two types of supplements are published by the respective awarding units. Those printed on yellow paper concern contracts: solicitations of sources and announcement of availability of requests for proposals. Those printed on blue paper concern invitations for grant applications in well-defined scientific areas to accomplish specific program purposes.

HE 20.3008/2:

NOTICE

Enforcement of Page Limitations on Grant Applications

The PHS 398 grant application kit has specific instructions on page limitations for certain parts of an application. The biographical sketch is limited to two pages. In the Research Plan, the "Specific Aims" section is not to exceed one page, the "Significance" section is not to exceed three pages, and the "Progress Report/Preliminary Studies" section is not to exceed eight pages (excluding the lists of professional personnel and publications and the appendix).

Over the past two years, the NIH has given the scientific community an opportunity to become accustomed to these page limitations, but the increasing workload now necessitates a firm stance. Starting with the October 1, 1982 receipt date, applications that exceed the above page limitations without the required brief explanation will be returned.

Please Conserve PHS 398 Forms

Each year the NIH distributes about 100,000 PHS 398 grant application kits, but only about 27,000 of these are returned as submitted applications. We don't know what happens to the other kits. We do know that each kit is expensive to print and mail, and that any funds saved by not wasting applications could be used elsewhere in the NIH system. In order to conserve forms and reduce costs, please follow these guidelines:

For applicant organizations:

- Be sure the staff in your application control office maintain a tighter control over the distribution of the application kits.

For investigators:

- If you have any extra PHS 398 grant application kits, don't save them or throw them away. Give them to colleagues to use or return them to your institution's application control office.

- When you need an application form, don't automatically phone the NIH. Check with your institution's application control office, for these offices have been sent copies of the PHS 398 kits in bulk for your use.

NOTICE

AVAILABILITY OF PUBLICATION ON ANIMAL MODELS FOR STUDYING DIABETES MELLITUS AND ITS COMPLICATIONS

NATIONAL INSTITUTES OF HEALTH DIABETES COORDINATING COMMITTEE

The National Institutes of Health Diabetes Coordinating Committee convened a task force to explore how existing or new animal models can be utilized to help answer problems about the etiology, pathogenesis, and underlying mechanisms of diabetes mellitus and its complications. Fifty-seven scientists, each a recognized expert in the field of diabetes mellitus research or animal genetics, were invited to contribute to this effort. During a four-month period, the participants thoroughly evaluated the available literature on animal models used in diabetes research. In the spring of 1981, the group assembled in Bethesda, Maryland, to discuss their findings. The task force's report was published as a supplement to Diabetes (Volume 31, Supplement 1, 1982) in April, 1982. A limited number of copies are available for distribution to interested scientists. To request a copy, please send a self-addressed label to:

Ms. Susan Stark
Attention: DIABETES
Publications Office
Fogarty International Center
Building 38A, Room 609
National Institutes of Health
Bethesda, Maryland 20205

ANNOUNCEMENT

UPDATE OF NEW INVESTIGATOR RESEARCH AWARD

PROGRAM INFORMATION

NIH awarding units may use the New Investigator Research Award (NIRA) to emphasize areas of investigation that are perceived to need special emphasis. Therefore, any proposal that does not fall within one of the listed areas will be returned. It is suggested that potential applicants contact one of the individuals listed below prior to submitting an application.

NIA: Research programs on aging support studies on the biological processes of aging at the cellular, tissue, body system and whole organism level; clinical research on the medical problems and diseases of the aged; and the social, cultural, economic and psychological factors affecting both the aging process and the status of older people in society.

Dr. Don Gibson
National Institute on Aging
Building 31, Room 5C06
(301) 496-5398

NIAID: Research with clinical relevance in virology, immunology, mycology and tropical diseases.

Dr. Luz A. Froehlich
National Institute for Allergy
and Infectious Diseases
Westwood Building, Room 704
(301) 496-7131

NIADDK: Research in the following program areas: diabetes, endocrinology, metabolism, digestive diseases, liver diseases, pancreatic diseases, nutrition, hematology, renal physiology, renal pathophysiology, urology, chronic renal diseases, arthritis, musculo-skeletal and skin diseases.

Dr. George Brooks
National Institute of Arthritis, Diabetes,
Digestive and Kidney Diseases
Westwood Building, Room 655
(301) 496-7277

For a complete description of the NIRA, see NIH Guide for Grants and Contracts, Volume 9, Number 1, January 3, 1980, p.67.

NCI: Research in cancer etiology, prevention, detection, diagnosis, treatment, restorative care and cancer biology.

Mr. Herman Fox
Grants Review Branch
Division of Extramural Activities
National Cancer Institute
Westwood Building, Room 826
(301) 496-5147

NICHD: Research relating to: Mothers and children (including pregnancy and infancy, developmental biology and nutrition, mental retardation, child and adolescent development); and Population (including reproduction, fertility-infertility, fertility control, social and behavioral aspects of reproduction, population change), with special interest in the social and behavioral aspects of population research.

Dr. Betty Pickett
National Institute of Child Health
and Human Development
Building 31, Room 2A04
(301) 496-1848

NIDR: Research in cariology, mineralization, craniofacial anomalies, nutrition, denta pain control, periodontal diseases, restorative materials, salivary secretions soft tissue diseases and selected behavioral studies.

Dr. George Hausch
National Institute of Dental Research
Westwood Building, Room 509
(301) 496-7748

NIEHS: Research in the general areas of epidemiology, identification of environmental hazards, development of test methods for risk assessment, pollutant pharmacokinetics in both the body and the external environment, and molecular and cellular mechanisms of damage. Special emphasis areas include physical factors, and, in particular, ionizing and non-ionizing irradiation; the effects of environmental agents on the endocrine system, digestion and nutrition; the synergistic and additive effects of smoking; the effects of environmental agents upon the immune system; and the development of rapid, reliable and inexpensive tests for toxicity.

Dr. Edward Gardner
National Institute of Environmental
Health Sciences*
Research Triangle Park, North Carolina
(919) 541-7724

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* Except as noted for NIEHS all Institutes are located in Bethesda, Maryland 20205

NEI: Research related to vision and disorders of the visual system: retinal and choroidal diseases, corneal diseases, cataract, glaucoma, strabismus, amblyopia and visual processing.

Dr. Ronald Geller
National Eye Institute
Building 31, Room 6A03
(301) 496-4903

NIGMS: Research in anesthesiology, trauma and burns.

Dr. Elizabeth O'Hern
National Institute of General
Medical Sciences
Westwood Building, Room 952
(301) 496-7001

NHLBI: Research in areas related to heart, blood vessel, lung, and blood diseases and blood resources.

Dr. Henry G. Roscoe
National Heart, Lung, and
Blood Institute
Westwood Building, Room 7A17
(301) 496-7225

NLM: Research in information science for representation of medical knowledge and its application to the health care system. Studies using computer based systems for information retrieval and application to actual problems confronting the health professional. Research in new methods of classifying, indexing and abstracting information for the organization of biomedical knowledge. Greater research in user needs and behavior and the properties of the user/system interface.

Dr. Roger Dahlen
National Library of Medicine
Federal Building, Room 902
(301) 496-4221

NINCDS: Research in basic and clinical neurosciences and in basic and clinical communicative sciences.

Dr. John W. Diggs
National Institute of Neurological and
Communicative Disorders and Stroke
Federal Building, Room 1016
(301) 496-4188

DRR: Research in the following technological areas: computer science applications in medicine, biomedical engineering, nuclear magnetic resonance, electron spin resonance, electron microscopy or biomedical kinetics. Research in laboratory animal sciences related to etiology, pathogenesis and control of laboratory animal diseases and environmental requirements of laboratory animals. Studies directed toward finding animal models of human disease.

Dr. Francis J. Kendrick
Division of Research Resources
Building 31, Room 5B05
(301) 496-5507

ANNOUNCEMENT

SMALL GRANT PROGRAM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
ALCOHOL, DRUG ABUSE, AND MENTAL HEALTH ADMINISTRATION
NATIONAL INSTITUTE OF MENTAL HEALTH
NATIONAL INSTITUTE ON DRUG ABUSE
NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM

The Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA) announces an increase in the direct cost limit for Small Grant Program applications to $15,000. Support is limited to a one-year period and is not renewable. This announcement is applicable to grants awarded after October 1, 1982 (the beginning of Fiscal Year 1983).

The ADAMHA Small Grant Program accepts applications that fall within the program interests of the National Institute of Mental Health (NIMH), the National Institute on Alcohol Abuse and Alcoholism (NIAAA), and the National Institute on Drug Abuse (NIDA). This program is primarily coordinated by the NIMH. However, each Institute makes awards for small grants relevant to its mission.

PURPOSE

The ADAMHA Small Grant Program provides relatively rapid financial support which is principally intended for newer, less experienced investigators, those at small colleges, and others who do not have regular research grant support or resources available from their institutions. Small grants may be used to carry out exploratory or pilot studies, to develop and test a new technique or method, or to analyze data previously collected.

The ADAMHA Small Grant Program invites applications for research grants which cover the entire range of scientific areas relevant to mental health, or to drug or alcohol abuse. While proposals may involve a wide variety of biomedical, behavioral and related disciplines, relevance to the missions of the ADAMHA Institutes must be present. Applications for studies aimed at problems outside these areas will not be accepted. Programmatic areas of interest are described in the documents listed on page 4 of this announcement. Potential applicants with questions concerning acceptability of their proposed work should contact the NIMH Small Grant Program, which is primarily responsible for coordinating the whole program.

LEGAL BASIS

This program is conducted under the authority of Section 301 of the Public Health Service Act (42 U.S.C. 241) and Section 501 of the Comprehensive Alcohol Abuse and Alcoholism Prevention, Treatment and Rehabilitation Act of 1970, as amended (42 U.S.C. 4585). Governing regulations are contained at 42 CFR Part 52. In addition, portions of the following regulations may also be relevant and applicable:

42 CFR 2 Confidentiality of Alcohol and Drug Abuse Patient Records

45 CFR 46 Protection of Human Subjects

The Animal Welfare Act of 1966 (Public Law 89-544) as Amended

45 CFR 74 Aministration of Grants

45 CFR 80 Nondiscrimination under Programs Receiving Federal Assistance through the Department of Health, Education, and Welfare Effectuation of Title VI of the Civil Rights Act of 1964

45 CFR 84 Nondiscrimination on the Basis of Handicap in Programs and Activities Receiving or Benefiting from Federal Financial Assistance

45 CFR 86 Nondiscrimination on the Basis of Sex in Education Programs and Activities Receiving or Benefiting from Federal Financial Assistance

45 CFR 91 Nondiscrimination on the Basis of Age in Programs and Activities Receiving or Benefiting from Federal Financial Assistance

Sections of the Code of Federal Regulations are available in booklet form from the U.S. Government Printing Office.

AVAILABILITY OF FUNDS

An estimated total of two million dollars is budgeted annually by the three ADAMHA Institutes for the support of the research grants described in this announcement.

ELIGIBILITY AND TERMS OF SUPPORT

Applications for small research grants may be submitted by any public or private, profit or nonprofit institution such as a university, college, hospital, laboratory, and units of State and local government.

Small grant support may not be requested to supplement research projects already being supported, or to provide interim support of projects under review by the Public Health Service. Simultaneous submissions of both a small and regular research grant application on the same topic will not be accepted. Small grant support may not be requested for thesis, or dissertation research.

Current Public Health Service regulations and policies for research project grants, including allowable direct costs, cost-sharing requirements, and indirect cost rates, also apply to ADAMHA small grants. Support for subsequent years may be requested through the regular research grant programs of the Public Health Service.

SUBMISSION PROCEDURES

Small grant applications may be submitted at any time and without regard to the receipt dates that pertain to the regular research grant program. However,

> APPLICATIONS REQUESTING EARLY SUMMER (JUNE) STARTING DATES MUST BE RECEIVED NO LATER THAN DECEMBER 1; APPLICATIONS WITH JULY AND AUGUST STARTING DATES MUST BE RECEIVED NO LATER THAN FEBRUARY 1.

Receipt Date by DRG	Initial Review	Council	Earliest Start Date
Early October	November	January	February 1 or March 1
December 1	January	May	May 1 or June 1
February 1	April	May	July 1 or August 1
Early May	June	September	Sept. or December 1
Early August	September	September	December 1

Applications will be processed as they are received and will be assigned to the next scheduled meeting of the Mental Health Small Grant Review Committee, which meets five times a year, followed by review by the National Advisory Mental Health Council, the National Advisory Council on Alcohol Abuse and Alcoholism, or the National Advisory Council on Drug Abuse. Approximately five months should be allowed between submission of the application and the desired starting date of the grant.

Application form PHS 398 (used in applying for other Public Health Service research grants) is used in applying for a small grant. Please indicate "ADAMHA Small Grant Program" in item 2 on the face page of the application. The forms should be completed according to the instructions accompanying the forms. It is suggested that inexperienced applicants ask a senior colleague for a critical reading prior to submitting the completed application. Application forms may be obtained from university sponsored research offices. Applicants from State or local governments should use application form PHS 5161. If not available, application forms may be requested from the NIMH Small Grants Program Office. Applications should be submitted to the following address:

Division of Research Grants
Westwood Building, Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205

REVIEW CRITERIA

All applications are reviewed by the Mental Health Small Grant Review Committee. The basic criteria for review of small grant applications include overall quality and scientific merit of the proposed research. Scientific merit involves considerations such as the research design, feasibility of the study, soundness of the approach, creativeness, and the qualifications and experience of the investigators. The availability of suitable facilities to perform the proposed studies, the supportive nature of the research environment, and the appropriateness of the proposed budget for the research program are also important evaluative factors.

AWARD CRITERIA

Criteria for funding of applications are the scientific merit of the proposal and the relevance to areas of interest described in each institute's research grant announcements. The availability of funds will also be considered in determining which awards will be made.

OTHER RELEVANT INFORMATION

For information about the Small Grant Program, as well as NIMH program announcements, please contact:

Dr. Ellen Simon Stover
Chief, Small Grants Program
National Institutes of Mental Health
Alcohol, Drug Abuse, and Mental Health
Administration
Parklawn Building, Room 10-104
5600 Fishers Lane
Rockville, Maryland 20857

Telephone: (301) 443-4337

FOR PROGRAM ANNOUNCEMENTS FOR NIDA AND NIAAA, PLEASE CONTACT:

NIDA Research Program Announcements
National Institute on Drug Abuse
Parklawn Building, Room 9-36
5600 Fishers Lane
Rockville, Maryland 20857

NIAAA Research Program Announcements
National Institute on Alcohol Abuse and Alcoholism
Parklawn Building, Room 14C-17
5600 Fishers Lane
Rockville, Maryland 20857

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11/7

NIH GUIDE for GRANTS and CONTRACTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Vol. 11, No. 7, June 18, 1982

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HAVE YOU MOVED?

If your present address differs from that shown on the address label, please send your new address to: Grants and Contract Guide Distribution Center, National Institutes of Health, Room B3BN10, Building 31, Bethesda, Maryland 20205, and attach your address label to your letter. Prompt notice of your change of address will prevent your name from being removed from our mailing list.

The GUIDE *is published at irregular intervals to announce scientific initiatives and to provide policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in grants and contracts activities administered by the National Institutes of Health.*

Two types of supplements are published by the respective awarding units. Those printed on yellow paper concern contracts: solicitations of sources and announcement of availability of requests for proposals. Those printed on blue paper concern invitations for grant applications in well-defined scientific areas to accomplish specific program purposes.

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NIH GUIDE FOR GRANTS AND CONTRACTS
Vol. 11, No. 7, June 18, 1982

NOTICE

SPECIAL EDITION

National Research Service Awards

Guidelines

for

Individual Awards - Institutional Grants

The administrative guidelines for the National Research Service Award program have been published as a special edition to this volume of the NIH Guide for Grants and Contracts. The guidelines have been revised to reflect the legislative changes enacted by the Omnibus Reconciliation Act of August 13, 1981 and other administrative changes.

Copies of the guidelines are being sent directly to the current program directors of institutional training grants, individual fellowship recipients, and the Business Offices and Sponsored Programs Offices of the grantee institutions that receive NRSA Support from NIH, ADAMHA, and HRA/DN.

Additional copies are available upon request from:

Office of Grant Inquiries
Division of Research Grants
National Institutes of Health
Westwood Building - Room 449
5333 Westbard Avenue
Bethesda, Maryland 20205

Telephone: 301 - 496-7441

NOTICE

ERRATA

An Announcement in the April 23, 1982 Guide for Grants and Contracts (Vol. 11, No. 5) entitled "Request for Research Grant Applications: RFA NIH-NIAID 82-8 Centers for Interdisciplinary Research on Immunologic Diseases, National Institute of Allergy and Infectious Diseases, was printed with an incorrect receipt date for applications. The correct application receipt date should be October 15, 1982.

NOTICE

Comments Invited on Alert Records

In accordance with the requirements of the Privacy Act, the Public Health Service (PHS) recently published notice of a new Privacy Act system of records, 09-25-0151, "Administration: Alert Records Concerning Investigations or Determinations of Misconduct by Current or Potential Recipients of Funds for Biomedical Research." PHS has also described routine uses for this system.

The full text of the notice may be found in the Federal Register, Vol. 47, No. 92, May 12, 1982, pages 20381-20383. Briefly, the system establishes a "flagging" procedure for incoming grant applications and contract proposals to enable the National Institutes of Health (NIH) to make informed decisions on appropriate actions regarding awards of research funds to individuals who are subjects of ongoing investigations of possible wrong-doing or have been shown to have engaged in misconduct. It establishes a procedure for alerting the directors of NIH awarding units whenever an individual who is under investigation requests funds, and provides for consideration of that information before a decision about an award is made. The system does not prohibit making an award when an investigation is underway but requires the Director of the awarding unit to consult with the NIH Associate Director for Extramural Research and Training prior to making a funding decision.

Access to information on pending investigations is strictly controlled. Staff who flag incoming requests do not know whether they are doing so for purposes of the alert or for other reasons. No information related to the alert is entered in the central NIH data base.

Please note that although the Federal Register notice establishes June 11, 1982, as the deadline for comments, NIH will accept comments until July 15, 1982, in order to accommodate readers of the Guide who may not have seen the Federal Register notice. Comments should be addressed to:

Dr. Kenneth Thibodeau
NIH Privacy Act Coordinator
Building 31 - Room 3B07
9000 Rockville Pike
Bethesda, Maryland 20205

Telephone: 301 - 496-4606

REANNOUNCEMENT

BIOMEDICAL RESEARCH SUPPORT SHARED INSTRUMENTATION GRANTS

DIVISION OF RESEARCH RESOURCES

Application Receipt Date: October 15, 1982

Council Date: June 1983

I. BACKGROUND

As part of its mission to create, develop, and maintain research resources needed by NIH-supported biomedical investigators throughout the nation, the Division of Research Resources (DRR) is continuing its competitive biomedical shared instrumentation grant program initiated in Fiscal Year (FY) 1982. The program was established in recognition of the long-standing need in the biomedical research community to cope with rapid technological advances in instrumentation and the rapid rate of obsolescence of existing equipment. The objective of the program is to make available, to institutions with a high concentration of NIH extramural research awards, research instruments which can only be justified on a shared use basis and for which meritorious research projects are described.

All unfunded applications submitted for the FY 1982 review cycle will be administratively withdrawn by the DRR, unless the applicant is notified to the contrary.

Eligible institutions may submit applications requesting the same, similar or different instrumentation for the FY 1983 review cycle.

II. RESEARCH GOALS AND SCOPE

This program is designed to meet the special problem of acquisition and updating of expensive shared-use instruments which are not generally available through other NIH mechanisms, such as the regular research, program project and center grant programs, the Biomedical Research Support (BRS) Grant Program and other DRR programs such as Animal Resources and the Biotechnology Resources Program. The latter program emphasizes development of the instrument and associated research methodology, research aspects which are not required in the new BRS Shared Instrumentation Program. The BRS Shared Instrumentation Program is intended for a broad community of NIH supported investigators.

This program is described in the Catalog of Federal Domestic Assistance No. 13.337, Biomedical Research Support. Awards will be made under the authority of the Public Health Service Act, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 42 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

III. ELIGIBILITY

The shared instrumentation grant program is a subprogram of the Biomedical Research Support (BRS) Grant Program of DRR. Awards are made under the authority of the BRS program and are made to institutions only, not to individuals. In FY 1983, eligibility is limited to those grantees which received a BRS grant award in FY 1982. NIH records will be used to verify eligibility. Only one application for a single shared instrument may be submitted by each eligible BRS grantee in a review cycle. Applications will be received only once per year. The program is highly competitive. Approximately $5.0 million have been requested for the program in FY 1983. At this funding level, it is expected that a minimum of 20 and a maximum of 66 awards would be made in 1983. Future funding is contingent on the availability of appropriated funds.

IV. MECHANISM OF SUPPORT

BRS Shared Instrumentation Grants provide support for expensive state-of-the-art instruments utilized in biomedical research. Applications are limited to instruments that cost at least $75,000 per instrument or system. Types of instrumentation supported include, but are not limited to, nuclear magnetic resonance systems, electron microscopes, mass spectrometers, protein sequencer/amino acid analyzers and cell sorters. Support will not be provided for general purpose equipment or "stand alone" computer systems.

Awards will be made for the direct costs of acquisition of new, or the updating of existing, research instruments. The institution must meet those costs (not covered in the normal purchase price) required to place the instrumentation in operational order as well as the maintenance, support personnel and service costs associated with maximum utilization of the instrument. There is no upper limit on the cost of the instrument, but the maximum award is $250,000. Grants will be awarded for a period of one year and are not renewable. Supplemental applications will not be accepted. The program does not provide indirect costs or support for construction or alterations and renovations. If the amount of funds requested does not cover the total cost of the instrument, an award will not be made unless the remainder of the funding is assured. Description of the proposed co-funding must be presented with the application. Assurance of co-funding, signed by an appropriate institutional official, must be presented to DRR prior to the issuance of an award. The shared instrument will not be transferable outside of the institution to which it is awarded.

A major user group of three or more investigators should be identified. Each major user must have NIH peer-reviewed research support at the time of the award. The application must show a clear need for the instrumentation by projects supported by multiple NIH research awards and demonstrate that these projects will require at least 75% of the total usage of the instrument. Major users can be individual researchers, or a group of investigators within the same department or from several departments at the applicant institution. NIH extramural awardees from other institutions may also be included.

If the major user group does not require total usage of the instrument, access to the instrument can be made available to other users upon the advice of the advisory committee. These users need not be NIH awardees but priority should be given to NIH-supported scientists engaged in biomedical research.

A progress report shall be required for three years. The report will cover the period August 1 through July 31 and be submitted within 30 days following the reporting period. The report must describe the use of the instrument, listing all users, and indicate the value of the instrumentation to the research of the major users and to the institution as a whole.

V. ADMINISTRATIVE ARRANGEMENTS

Each applicant institution must propose a Principal Investigator who can assume administrative/scientific oversight responsibility for the instrumentation requested. An internal advisory committee to assist in this responsibility should also be utilized. It is expected that in most cases, the BRS Program Director and extant BRS advisory apparatus, augmented with members having technical and scientific expertise regarding the instrumentation requested, can serve this function. However, there may be circumstances where other existing or proposed arrangements are more appropriate for the applicant institution.

In any event, the Principal Investigator and the advisory group are responsible for the development of guidelines for shared use of the instrument, for preparation of all reports required by the NIH, for relocation of the instrument within the grantee institution if the major user group is significantly altered and for continued support for the maximum utilization and maintenance of the instrument in the post award period.

A plan should be proposed for the day-to-day management of the instrument including designation of a qualified individual to supervise the operation of the instrument and to provide technical expertise to the users. Specific plans for sharing arrangements and for monitoring the use of the instrument should be described.

VI. REVIEW PROCEDURES AND CRITERIA

Applications are reviewed by specially convened initial review groups of the Division of Research Grants for scientific and technical merit and by the BRS Subcommittee of the General Research Support Review Committee and the National Advisory Research Resources Council of the Division of Research Resources for program considerations. Funding decisions are the responsibility of the Division of Research Resources and will not be made prior to June 15, 1983.

Criteria for review of applications include the following:

1. The extent to which an award for the specific instrument would meet the scientific needs and enhance the planned research endeavors of the major users by providing an instrument that is unavailable or to which availability is highly limited.

2. The availability and commitment of the appropriate technical expertise within the major user group or the institution for use of the instrumentation.

3. The adequacy of the organizational plan for administration of the grant including sharing arrangements for use of the instrument.

4. The institution's commitment for continued support of the utilization and maintenance of the instrument.

5. The benefit of the proposed instrument to the overall research community it will serve.

VII. METHOD OF APPLYING

A. Application Format

Applications are to be submitted on the standard PHS research grant application form (PHS-398, Rev. 5/80) available from most institutional business offices or the Division of Research Grants, NIH. Instructions supplied with these forms should be followed except for the following;

1. Face page of the application
   - a. Item 1. The instrument requested should be named in the title of the proposal.
   - b. Item 2. Write in "DRR-BRS SHARED INSTRUMENTATION GRANT"
   - c. Item 6. Write in August 1, 1983 - July 31, 1984.
   - d. Item 12. Complete Item 12 and type in the institution's BRS grant number.

     (Note at the bottom of the page if a duplicate application has been sent to another agency.)
2. Application page 2. Identify the Principal Investigator, the major user group and the complete grant number(s) for each of the users currently active NIH research support.
3. Application page 4. A detailed breakdown of the direct costs requested will be shown on the budget page. Provide a complete description of the instrument including manaufacturer, model number and cost including tax and import duties, if applicable. If possible, the model chosen should be justified by comparing its performance with other available instruments.
4. Application page 5. Budget Estimates for All Years. Not applicable; do not submit.
5. Biographical Sketch. In addition to the personnel listed on page 2, include a biographical sketch of the person(s) who will be in charge of maintenance and operation of the instrument and a brief statement of the qualifications of the individual. Biographical sketches should not exceed 2 pages for each individual.

Section 2 of the application. Provide information relative to the points identified under criteria for review including:

1. A description of similar instruments existing at the institution or at nearby institutions and a justification why new or updated

equipment is needed. A clear justification should be given for the choice of the instrument and ancillary accessories requested.

2. A description, by major users, of the research projects for which the instrumentation is required. The descriptions need not be of the detail of a regular research grant application (should not exceed 4 pages) but should point out the benefit of the proposed instrument to the research objectives of each major user. An estimate of the percentage use of each project should be given. If there are more than 4 major users, set up a table listing the names of the users, the NIH grant number, the estimated percentage use and the title of each research project.

3. A description of the organizational plan for administration of the grant.

4. A specific plan and a staement of institutional commitment to operate and maintain the instrument for its useful life at the same utilization level after termination of the 3-year reporting period to DRR.

B. Application Procedure

Applications must be received by October 15, 1982. Applications received after this date will not be accepted for review in this competition. The original and six copies should be sent to:

Application Receipt Office
Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205

Inquiries and three copies of the application should be addressed to:

Biomedical Research Support Grant Program
Division of Research Resources
National Institutes of Health
Building 31 - Room 5B23
Bethesda, Maryland 20205

ANNOUNCEMENT

LONG-TERM EFFECTS OF CRANIOFACIAL INJURIES

NATIONAL INSTITUTE OF DENTAL RESEARCH

The National Institute of Dental Research (NIDR) invites applications for support of research related to the long-term effects of traumatic injury to the craniofacial structures.

Each year, approximately 10.5 million persons in the United States suffer a facial or head injury requiring medical care or restriction of activity for a period of time. This number is about five percent of the total population. Many of these injuries result from vehicular trauma, thermal burns and gunshot wounds. Athletics, falls, dog bites and interpersonal violence are also known to contribute to the problem.

It is not known, however, what proportion of craniofacial injuries result in long-term or permanent disfigurement or loss of function. Similarly, data are sparse or lacking entirely on the sources of injuries, the nature of injuries, the kinds of medical treatment required, the costs of such treatment, and the psychosocial consequences of these injuries and defects to the patient and his or her family.

Investigators able to conduct studies to obtain the desired data or who have access to the kinds of data being sought are encouraged to submit a grant application to the NIDR. The deadlines for the receipt of research grant applications by the Division of Research Grants are March 1, July 1, and November 1. Review and award of such applications will be through the usual NIH procedures governing research project grants. The award of grants pursuant to this announcement is contingent upon the receipt of responsive proposals of high scientific merit and the availability of appropriated funds.

Inquiries regarding this announcement may be directed to:

Dr. Jerry D. Niswander or
Dr. John D. Suomi
Craniofacial Anomalies Program Branch-EP
National Institute of Dental Research
National Institutes of Health
Westwood Building - Room 520
Bethesda, Maryland 20205

Telephone: 301 - 496-7807

This program is described in the Catalog of Federal Domestic Assistance No. 13.842, Craniofacial Anomalies. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject A-95 Clearinghouse or Health Systems Agency review.

ANNOUNCEMENT

MULTIPURPOSE ARTHRITIS CENTERS

NATIONAL INSTITUTE OF ARTHRITIS, DIABETES, AND DIGESTIVE AND KIDNEY DISEASES

Guidelines have been revised for applications for Multipurpose Arthritis Center grants. This announcement by the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases (NIADDK) supersedes all previous announcements for Multipurpose Arthritis Centers published in the NIH Guide to Grants and Contracts. The revised guidelines for preparing an application for a Center grant are immediately available. These guidelines update the policies governing the Multipurpose Arthritis Centers program. They will become effective beginning June 1982 and will apply to both new and competing continuation applications.

Multipurpose Arthritis Center Grants are awarded under authority of Section 439 of the Public Health Service Act as enacted by the National Arthritis Act of 1974 (42 U.S. Code Sec. 289 c-6).

A Multipurpose Arthritis Center is defined as a resource which consists of the facilities of a single institution or a consortium of cooperating institutions through which a group of formally cooperating health personnel can be brought together to develop new knowledge and to demonstrate and foster the prompt and effective application of available knowledge.

As described in the National Arthritis Act, Multipurpose Arthritis Centers shall carry out the following:

1. Conduct basic and clinical research into the cause, diagnosis, control, and treatment of arthritis and complications resulting from arthritis, including research into implantable biomaterials and biomechanical and other orthopedic procedures, and in the development of other diagnostic and treatment methods.

2. Conduct training programs for physicians and other health and allied professionals in current methods of diagnosis, control, and treatment of arthritis, and in research in arthritis.

3. Conduct information and continuing education programs for physician and other health and allied health professionals who provide care for patients with arthritis.

4. Conduct programs for the education of patients, and for the dissemination of information to the general public.

The funds awarded as a Multipurpose Arthritis Center Grant are in support of an Arthritis Center. They are not intended as the total or even necessarily most of the funds used by the Center to accomplish its programs. Instead, funds provided by the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases are to be used to coordinate existing activities and to develop new capabilities for progress in rheumatic disease research, education, and community activities at the host institution.

Each Center will have three major operating components: Research, Education, and Community/Health Services Research programs. In addition, each Center will include an Administrative Unit concerned with planning, development, administration, and maintenance of an active and unified Center.

The Center grant may also include support for: 1) developmental and feasibility studies; and 2) core units.

All applications should be prepared in accordance with the revised guidelines dated May 1982. In order to facilitate Institute planning, the NIADDK must receive a letter of intent describing the proposed Arthritis Center. The letter should be received no later than four months before the anticipated submission date of the application. Letters of intent are applicable to both new and competing continuation applications. Applications not preceded by a letter of intent four months prior to the receipt date will be returned.

Consultations between NIADDK staff and potential applicants prior to submission of the formal application are encouraged. Applicants are requested to make arrangements for such consultation early in the application process. It is understood that staff will not be evaluating the merit of the proposal.

A letter of intent is not binding and will not enter into the review of any proposal subsequently submitted.

Receipt dates for applications and respective letters of intent are:

Letter of Intent	Application
October 1	February 1
February 1	June 1
June 1	October 1

The National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases plans to make awards for the Centers program contingent upon the appropriation of funds and in accordance with appropriate peer review.

Copies of the revised guidelines and further information about the Multipurpose Arthritis Centers program are available from, and letters of intent should be addressed to:

Multipurpose Arthritis Center
Program Director
National Institute of Arthritis, Diabetes,
and Digestive and Kidney Diseases
National Institutes of Health
Westwood Building - Room 403
Bethesda, Maryland 20205
Telephone: 301 - 496-7495

NOTICE

PROGRAM PROJECT AND CENTER APPLICATIONS PRE-APPLICATION PROCEDURES

NATIONAL INSTITUTE OF ARTHRITIS, DIABETES, AND DIGESTIVE AND KIDNEY DISEASES

This notice is intended to inform prospective new applicants for NIADDK program project and center grants of pre-application procedures.

Letter of Intent: In order to facilitate Institute planning and to provide prospective applicants with advice concerning the preparation of their applications, the NIADDK, beginning with the February 1, 1983 receipt date, will require that applicants submit a letter of intent at least four months prior to submission of an application. The letter should include a brief description of the proposed program project or center including participants and their areas of expertise and an estimate of the requested level of support. This letter of intent is not binding upon any prospective applicant. However, prospective applicants should note that applications not preceded by a letter of intent four months prior to the receipt date will be returned.

Pre-Application Conference: The NIADDK strongly believes that consultation between Institute staff and prospective applicants is essential prior to submission of an application, and suggests that such consultation occur early in the application planning process. Applicants should not construe advice given by the Extramural Program staff as assurance of favorable review. The staff will not evaluate or discuss the merit of the scientific aspects of the proposal.

Letters of intent and inquiries should be addressed as follows:

For Diabetes Research and Training Centers and
Diabetes, Endocrinology Research Centers:

Diabetes Centers Program Director, DEMD
National Institute of Arthritis, Diabetes, and
Digestive and Kidney Diseases
Bethesda, Maryland 20205

Telephone: 301 - 496-7418

For Multipurpose Arthritis Centers:

Multipurpose Arthritis Centers Program
Director, AMSD
National Institute of Arthritis, Diabetes, and
Digestive and Kidney Diseases
Bethesda, Maryland 20205

Telephone: 301 - 496-7495

For Clinical Nutrition Research Units:

Nutrition Program Director, DDN
National Institute of Arthritis, Diabetes, and
Digestive and Kidney Diseases
Bethesda, Maryland 20205

Telephone: 301 - 496-7823

For all other Centers or Program Projects:

Director, Division of Extramural Activities
National Institute of Arthritis, Diabetes, and
Digestive and Kidney Diseases
Bethesda, Maryland 20205

Telephone: 301 - 496-7277

PREVENTIVE INTERVENTION RESEARCH CENTERS

ALCOHOL, DRUG ABUSE, AND MENTAL HEALTH ADMINISTRATION

NATIONAL INSTITUTE OF MENTAL HEALTH

BACKGROUND

A critical need exists to stimulate and support prevention research, especially research aimed at developing demonstrably effective, well-evaluated, early preventive intervention program models which subsequently can be adapted, replicated, and further refined as a result of the experience of prevention program practitioners.

A distinction must be made between basic or generative (i.e., non-intervention) sources of knowledge and actual or applied preventive intervention programs. The basic research knowledge base for early preventive interventions is large and rooted in diverse sciences and disciplines, and though far from complete, enough is now known for a variety of early preventive intervention efforts to be pursued.

Because Federal funds to support prevention research in mental health are limited, it has been decided to target activities to the development, implementation, evaluation, and dissemination of effective early intervention prevention program models. Preventive Intervention Research Centers (PIRCs) are proposed as a key NIMH-sponsored mechanism for developing and advancing knowledge on early preventive interventions. NIMH is accepting applications for the support of Preventive Intervention Research Centers.

The basic purpose of the Preventive Intervention Research Centers (PIRCs) program is to support the development and maintenance of a productive research environment, in a clinical, academic, or community setting, or an appropriate collaborative relationship between two or more such settings. Behavioral and clinical research scientists, clinicians, and prevention specialists can interact in such an environment and conduct high quality research on problems concerned with early interventions aimed at the prevention of mental illness, significant psychological dysfunction, and/or emotional disturbance among populations at risk.

This announcement defines early preventive intervention as (1) actions taken while it is still possible to either anticipate or reverse an early pathological/maladaptive process, and (2) such interventions occur in time prior to the need for treatment and/or rehabilitative services. The aim of preventive intervention research is to test empirically the benefits of systematic attempts to modify those factors which lead to specific mental disorders, significant psychological dysfunction and/or emotional disturbance. Such interventions are not limited to any age group(s) and may be applicable throughout the life span. Populations at risk refers to groups whose members evidence attributes which are associated with a higher probability of future disorders.

This program is described in the Catalog of Federal Domestic Assistance No. 13.242, Mental Health Research Grants. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

I. PROGRAM SPECIFICATIONS

A. PROGRAM OBJECTIVE

The objective of this program announcement is to encourage and stimulate high quality research on early preventive interventions for specific populations known to be at high risk for mental/emotional disorder. Integral to that objective, the intent of grants for Preventive Intervention Research Centers (PIRCs) is to support the growth and foster the productivity of problem-focused, multidisciplinary programs of early preventive intervention research.

The following operating framework provides a guide for characterizing appropriate early preventive intervention activities:

1. There is a knowledge base derived from existing research sufficient to support an early preventive intervention research effort;
2. Existing research data indicate that it is possible to identify groups not yet experiencing the specific significant dysfunction, but who are at high risk for developing these dysfunctions;
3. There is significant potential for achieving the main objective of early intervention, namely, preventing the occurrence of mental/emotional disorders or maladaptive psychological conditions.

B. CENTER CHARACTERISTICS

There is no prescribed model for these Centers. To give substance to the definition of a PIRC, however, the following characteristics must be present in each:

1. Each Center will provide an environment which assures the highest quality research and leadership in its chosen area of investigation. Through its activities, the Center should be regarded as a major research center by the surrounding scientific and clinical communities and, in time, might well become a regional or national research resource.
2. The program of each Center must be problem-oriented and multidisciplinary. Each Center must formulate a research program around a specific, clearly defined mental health problem or set of problems of major scientific and public health importance, such as the mental health/physical health interface, stress in the workplace, the psychological/physical environmental interface, the prevention of specific childhood disorders, or stress in the family.
3. The Principal Investigator will be the Director of the Center, who provides leadership for the scientific program and has final responsibility for the scientific, administrative, and operational aspects of the Center. He/she is responsible for the overall development of the Center as a valuable resource to the parent institution and to the scientific and clinical communities. The Director should be a

focuses on early preventive interventions in connection with the prevention of specific disorders. Problem areas within this category will frequently (but not always) meet relevant diagnostic criteria in DSM-III or ICD-9.

2. Preventing psychological dysfunction.

   a. Among populations which are at high risk as a function of severely debilitating developmental circumstances or other multiple causes.

   b. Among populations which have experienced significant acute transitional life crises and/or stressful life event(s) expected to increase the probability of pscyhopathological disorders.

When appropriate, the intervention modalities may be both preventive and promotive in that the intended outcomes aim toward both a reduction in rates of future disorders and the enhancement of specified aspects of mental health, and may have psychological, biological, or environmental components. Many types of program emphases and intervention modalities are appropriate as long as they are consistent with the types of problems cited above and the spirit of early preventive interventions cited earlier.

II. APPLICATION REQUIREMENTS

A. The research plan section of the application must include (Asterisks relate to Sections A-D, Research Plan, in the Specific Instructions of the application packet.):

   1. A five-year research plan. This plan should include an introductory section which specifies problem focus, intervention strategies, rationale for these in terms of the framework described on page 2, and specific research approaches. For each project in the research plan, the applicant should (a) present a scholarly summary of the existing knowledge base, sufficient to justify the merit and importance of the proposed intervention, (b) specify the objectives, characteristics, staffing, magnitude, and target groups for the proposed intervention, (c) specify time frames and anticipated activities, (d) describe the design and the methodological approaches to be used in assessing and analyzing data on the effects of interventions, (e) specify the meaning and potential impact of findings, and discuss the cost-effectiveness of the intervention(s) proposed for study, and (f) attend both to the effects of relevant demographic characteristics (e.g., age, sex, social class, ethnicity, etc.) of the at-risk target groups, and to developmentally relevant methodology for the age range of the groups to be studied. Applicants should also describe the types of further programmatic steps that might be taken in later years to build upon and elucidate early findings.*

   2. A plan for dissemination of program/research findings.*

knowledgeable, experienced research investigator with appropriate administrative skills who will assure the highest standards of investigation.

4. The Center is expected to have an administrative structure that will assure maximum effectiveness and efficiency of operation and sound financial practices. The administration will be responsible for program planning, monitoring, and execution, as well as preparation of the budget, control of expenditures, staff appointments, etc. A Center should have sufficient authority to establish the necessary administrative and management procedures for carrying out its total responsibility.

5. Each Center should have sufficient collaboration with community agencies (for example, a community mental health center) and with relevant departments and professional schools to carry out preventive intervention research.

6. The primary purpose of each Center is to carry out early preventive intervention research. An important byproduct of the research effort is the development of research competencies in promising scientists in the complex techniques and advanced theories of mental health preventive intervention research. Accordingly, each Center will provide research experiences for at least two preceptees annually, to be selected from the mental health and related disciplines. Precepteeships are defined as supervised work experience. Each Center should relate functionally with relevant departments of professional and graduate schools, as may be appropriate to the needs of the preceptees.

7. Each Center's overall program plan must include appropriate dissemination activities as research findings emerge, for example: (a) preparing manuscripts for publication in appropriate scientific and professional outlets, (b) preparing detailed program manuals and program evaluation guides, (c) providing consultation to agencies and groups seeking to develop early preventive intervention programs, and (d) participating and taking leadership conjointly with other PIRCs in workshop, conferences, and meetings designed to share established early preventive intervention technology and knowledge with other researchers and interested agencies and groups.

Each proposed activity within the total research program must conform both to the problem focus and to the operating framework stated above as a guide for early preventive interventions. Early preventive interventions may be directed to high-risk populations of any age, sociodemographic, or ethnic group, and may use a variety of intervention strategies.

C. PROBLEM AREAS

Problem areas for early preventive intervention research may include relatively low incidence but severe disorders or high incidence but relatively less debilitating disorders, or dysfunctions. Illustrative problem areas include:

1. Preventing specific psychopathologies or disorders. This approach

3. A description of the administrative organization and of the Center, including its relationship to the applicant institution, and arrangements for planning, coordinating, and evaluating the Center programs.*

4. A plan for selection, activities, and supervision of research preceptees, including delineation of relationships with appropriate departments of professional and graduate schools to serve as resources for the development of research scientists in early intervention research.*

5. In Section H of the PHS 398 application, there should be a description of the interest, support, cooperation, and nature of existing and proposed collaboration of community agencies or other entities or settings within which proposed intervention programs are to be conducted. Documentation of such arrangements should be included in appendices.

B. The biographical sketches must include:

1. Evidence that the Principal Investigator has an established record of productive involvements in preventive intervention research and program development. Also, that he/she will devote a substantial portion of time (e.g., thirty percent or more) to administrative, program development, research supervisory, and writing activities essential to a PIRC's effective program development.

2. A demonstrated history for other participating researchers of early preventive intervention research, as evidenced, for example, by ongoing project grant support and publications.

C. The budget section must include, in the justification, estimated percentages of first-year and total costs by budget category for (a) core program costs, and (b) associated costs with each specific research project.

III. PRE-APPLICATION CONSULTATION

For NIMH staff to provide early and targeted pre-application consultation, potential applicants are encouraged to submit a letter of intent, no longer than 12 pages, to the PIRC program[1] at least four weeks prior to initial submission of an intended PIRC grant application. The letter should summarize the present state of planning and development for establishing the proposed Center by providing the following information:

1. The Center's objectives.

2. A brief description of the problem focus, and the operational and research plans and methods to be used to reach the objectives of the program.

---

[1] Preventive Intervention Research Centers Program
National Institute of Mental Health
Parklawn Building - Room 18-105
5600 Fishers Lane
Rockville, Maryland 20857

3. A chart showing the institutional organization of the Center and its relationship to the applicant institution and, where relevant, to other community facilities.

4. An estimated first-year budget for the Center. (Use page 3 of a regular research grant application for a guide.) List the staff--names and to-be-named--who will participate in the Center, including titles, research roles, disciplines of investigators, their vitae, and percentage of time. Include an estimate of the level of support staffing.

5. Current and pending research, and research training grant support from all sources which will be available to the Center program.

6. Information about resources and facilities currently available to the Center.

Appropriate NIMH staff will be assigned to study each letter of intent, to review the preliminary plan, and to consult with prospective applicants to provide information regarding program relevance and purpose in order to help applicants comply with administrative requirements, meet program standards, and provide sufficient information to permit an adequate scientific merit review.

IV. PROCEDURES FOR REVIEW OF APPLICATIONS

Applications submitted in response to this Announcement will be reviewed on a nationwide basis in accord with the usual Public Health Service peer review procedures for research grants. They will be reviewed for scientific and technical merit by a review group composed primarily of non-Federal scientific experts (Initial Review Group) and by the National Advisory Mental Health Council. By law, only applications recommended for approval by Council will be considered for funding.

V. CRITERIA FOR REVIEW BY INITIAL REVIEW GROUP

A. Factors to be considered in evaluating applications include, but are not limited to:

   1. Adequacy of the conceptual and theoretical framework for the overall research program and specific components, including adequacy of research base to indicate the existence of, ability to identify, and potential for successful intervention with groups at risk for specific mental disorders or other significant psychological dysfunction, and/or emotional disturbance.

   2. Scientific merit of the research design, approaches, and methodology, including:

      a. Quality of a PIRC's specific plans for early preventive interventions, using a variety of intervention strategies consistent with a specific problem focus.

      b. Adequacy of the research methods and data analysis plans.

   c. Qualifications and experience of the investigative team.

   d. Adequacy of the existing and proposed facilities, resources, and administrative structure for achieving the proposed objectives.

   e. Feasibility of the research activities in terms of documentation of needed cooperation from service providers/agencies.

3. Potential for Center demonstrating a leadership role in early preventive intervention research.

4. Potential replicability of the proposed interventions.

5. Adequacy of protection of human subjects.

6. Availability of, or prospects for, individual investigators to secure and/or have project grant support.
7. Appropriateness of the budget, staffing plan, and time frame to complete the research.

8. Capacity of the applicant to provide research precepteeships.

9. Anticipated cost-effectiveness of the interventions.

10. Adequacy and appropriateness of the plan for dissemination of research findings.

VI. AWARD DECISION CRITERIA

A. The following criteria will be used in the decision to make an award for an application which has been recommended for approval, provided the applicant has complied with all legislative, regulatory, and policy requirements of the Public Health Service:

   1. Quality of the research program as determined during the review process.

   2. Programmatic relevance of the proposed research program, including consideration of types of populations being addressed, interventions, and strategies.

   3. Highest priority will be given to funding research programs on early interventions addressed to individuals in "at-risk" populations who have not evidenced the psychopathology which is the target of the preventive interventions.

   4. Potential for direct applicability of the research.

   5. Availability of funds.

VII. PROGRAM INFORMATION

Potential applicants may receive consultation concerning submission of applications in response to this Special Announcement by contacting:

Juan Ramos, Ph.D.
Director, Division of Special
Mental Health Programs
National Institute of Mental Health
Parklawn Building - Room 18-105
5600 Fishers Lane
Rockville, Maryland 20857

Telephone: 301-443-3533

In view of the special significance of this program, an NIMH staff member will have the responsibility for monitoring each supported Center and for continuing liaison with the Center Director.

VIII. APPLICATION INFORMATION

A. ELIGIBILITY REQUIREMENTS

These grants are available to any public or private, profit or non-profit institution such as a university, college, hospital, or community agency, including community mental health centers, and units of State or local governments and authorized units of the Federal Government.

B. FUNDING AND TERMS OF SUPPORT

Funds estimated at about $800,000 will be available in FY 83 to support applications submitted in response to this Announcement. It is anticipated that up to four awards will be made for PIRCs in FY 83. Applications may request a maximum period of five (5) years of support.

Grants are awarded directly to the applicant institution. Grant funds may be used only for those expenses which are directly related to and necessary to carry out research projects and must be expended in conformance with the Public Health Service Grants Policy Statement, applicable Federal regulations, and conditions set forth in this Announcement and on the grant award document. In general, grant funds may be used for: (1) direct costs which are necessary to carry out the project, including salaries, consultant fees, supplies and equipment, and essential travel; and (2) actual indirect costs to cover related overhead.

Funds may be requested for staff training and/or services only to the extent necessary to carry out the research and not available from other sources, and must be specifically justified.

C. APPLICATION PROCEDURES

Applicants should use Form PHS 398 (Rev. 5/80). State and local government agencies should use Form PHS 5161. Application kits may be obtained from the grants office of a university or are available from the following:

Grants Operation Section
National Institute of Mental Health
Parklawn Building - Room 7C-05
5600 Fishers Lane
Rockville, Maryland 20857

Telephone: 301 - 443-4414

Instructions for applicants are included in the kit. The phrase "PREVENTIVE INTERVENTION RESEARCH CENTER" should be entered in item #2 of the face page of the Application Form PHS 398 or item #7 of the face page of Form PHS 5161

The signed original and six copies of the application should be sent directly to the following address:

Division of Research Grants
National Institutes of Health
Bethesda, Maryland 20205

D. RECEIPT, REVIEW, AND AWARD SCHEDULE

Applications Received by:	Review Committee	Council	Earliest Possible Funding
November 1 *	February/March	May	July 1
March 1	June	September	December 1
July 1	October/November	January/February	April 1

* Applications submitted for the November 1, 1982 deadline will be considered for funding in FY 1983

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U.S. Department of Health and Human Services

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NATIONAL RESEARCH SERVICE AWARDS

Guidelines

for

Individual Awards - Institutional Grants

Public Health Service

National Institutes of Health

Alcohol, Drug Abuse, and Mental Health Administration

and

Division of Nursing, Health Resources Administration

HE 20. 3008/2:

NATIONAL RESEARCH SERVICE AWARDS

Guidelines

for

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June 18, 1982

Public Health Service

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Division of Nursing, Health Resources Administration

For Administrative Use Only

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GUIDELINES FOR NATIONAL RESEARCH SERVICE AWARDS

A. BACKGROUND

Under authority of Section 472 of the Public Health Service Act (42 USC 2891-1) as amended, the National Institutes of Health (NIH), the Alcohol, Drug Abuse and Mental Health Administration (ADAMHA), and the Division of Nursing, Health Resources Administration (DN) provide National Research Service Awards to individuals for training in specified areas of biomedical and behavioral research at public and non-profit private institutions including Federal laboratories. NIH, ADAMHA, and DN also make NRSA grants to domestic public and non-profit institutions for the research training of individuals selected by the institutions. The National Research Service Award legislation requires recipients of support to payback the Federal Government by engaging in health related biomedical or behavioral research and/or teaching. (See Section E. for details.) Title 42 of the Code of Federal Regulations, Part 66, is applicable to these awards.

1. Individual National Research Service Awards (Fellowships)

National Research Service Awards (NRSA) are made to individual fellowship applicants selected for award as a result of national competition for research training in specified health-related areas. NIH makes individual awards only at the postdoctoral and senior levels. NIH does not support individual predoctoral fellows except through the Minority Access to Research Careers program, which is announced separately. ADAMHA and DN make individual awards at both the predoctoral and postdoctoral level.

The application must clearly indicate the applicant's arrangements for sponsorship by a public or non-profit institution or a Federal laboratory that has the staff and facilities suitable to provide the proposed training. Under exceptional circumstances an individual may request support for training abroad. In such cases, the applicant is required to provide detailed justification based on the nature of the facilities and/or training opportunity and the particular suitability of the foreign situation, rather than the domestic, to the proposed research. The justification is evaluated in terms of the scientific advantages of the foreign training as compared to training available domestically. Only in cases where there are clear scientific advantages will the foreign training be approved.

Each applicant must (a) submit an application using forms provided by the appropriate agency (see Section B.2.) and (b) arrange for submission of references on his or her behalf. The major emphasis of the application should be the research training experience and broadening of scientific competence. Postdoctoral applicants requesting training at their doctoral degree granting or current training institution should explain in the application why further training at that institution would be valuable. The application must include the sponsor's Facilities and Commitment Statement and the applicant's signed statement that he or she has read the payback information and will meet the service or payback provisions required under the law as a condition for accepting the National Research Service Award. An individual may not have two competing NRSA applications pending review concurrently in the National Research Service Award program.

2. Institutional National Research Service Awards (Training Grants)

A domestic public or non-profit private institution may apply for a grant to support a research training program in a specified area(s) of research. Support for predoctoral and/or postdoctoral trainees may be requested. Each applicant institution must submit an application according to instructions, using forms provided by the appropriate agency (see Section B.2.).

The applicant institution must have the staff and facilities required for the proposed program. The training program director at the institution will be responsible for the selection and appointment of trainees and the overall direction of the training program. In selecting trainees, the program director must make certain that individuals receiving support meet the eligibility requirements set forth in these guidelines.

B. GENERAL PROVISIONS

1. Eligibility

a. Research Areas National Research Service Awards may be made for research training in areas which fall within the mission of NIH, ADAMHA, or HRA/DN as indicated in their program announcements. Applications which do not fit these guidelines will be returned.

An increased emphasis has been placed on the research training of physicians. The Secretary is required by law, in taking into account the Nation's overall needs for biomedical research personnel, to give special consideration to physicians who agree to undertake a minimum of two years of biomedical research.

b. Research Training Program The National Research Service Award must be used to support a program of research training. The NRSA may not support studies leading to the M.D., D.O., D.D.S., D.V.M., or other similar professional degrees; nor to support residencies, the primary purpose of which is the attainment of a medical or nursing specialty. Research trainees in clinical areas are expected to devote their time to the proposed research training and to confine clinical duties to those which are a part of the research training.

c. Degree Requirements

(1) Predoctoral Individuals, trainees or fellows, must have received, as of the beginning date of their NRSA appointment, a baccalaureate degree and must be training at the postbaccalaureate level in a program leading to the award of a doctor of philosophy of science or equivalent degree. Predoctoral fellows supported by ADAMHA must also have completed two or more years of graduate work and be enrolled in a doctoral degree program as of the proposed activation date. A predoctoral applicant to the Division of Nursing must be a registered professional with a baccalaureate or master's degree in nursing.

(2) Postdoctoral Individuals must have received, as of the beginning date of the NRSA appointment, a Ph.D., M.D., D.O., D.D.S., D.V.M., O.D., D.P.M., Sc.D., D. Eng., D.N.S., or equivalent domestic or foreign degree.

(3) Senior Fellows As of the beginning date of their award, senior fellows must have received a doctoral degree (as in B.1.c.(2) above) and must have had at least seven subsequent years of relevant research and professional experience. The senior fellowship is awarded by NIH to provide opportunities for experienced scientists to make major changes in the direction of their research careers, to broaden their scientific background, to acquire new research capabilities, or to enlarge their command of an allied research field. In addition, these awards will enable individuals beyond the new investigator stage to take time from regular professional responsibilities for the purpose of increasing their capabilities to engage in health-related research.

d. Citizenship The individual to be trained must be a citizen or a non-citizen national of the United States or have been lawfully admitted for permanent residence at the time of application for individual applicants or at the time of appointment in the case of an institutional award. A non-citizen national is a person who, although not a citizen of the United States, owes permanent allegiance to the U.S. They are generally persons born in lands which are not States, but are under U.S. sovereignty, jurisdiction, or administration (e.g., American Samoa). An individual lawfully admitted for permanent residence must submit a notarized statement, upon activation of the award, indicating possession of the alien registration receipt card (I-151 or I-551). Individuals on temporary or student visas are not eligible for support from the NRSA.

2. Applications and Receipt Dates

NIH application kits containing forms, instructions, and related information may be obtained from Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20205, 301-496-7441. National Institute of Mental Health, National Institute on Alcohol Abuse and Alcoholism, or National Institute on Drug Abuse application kits are available from the appropriate ADAMHA component Grants Management Branch, 5600 Fishers Lane, Rockville, Maryland 20857. Division of Nursing information and applications are available from the Division of Nursing, Health Resources Administration, Center Building, 3700 East West Highway, Hyattsville, Maryland 20782. The application for the institutional training grant is form PHS 6025. The application for the individual fellowship is form PHS 416-1. These application forms are also usually available at institutional Offices of Sponsored Research, Grants and Contracts Offices, or their equivalent.

Applicants are encouraged to submit applications well in advance of the published application receipt dates to allow sufficient time to provide any supplemental information which may be required. Application receipt dates are widely publicized in NIH, ADAMHA, and HRA/DN announcements. Applications received too late for one review will be considered at the next published review cycle.

3. Review

Each initial application will be evaluated for scientific merit by a PHS peer review group. Institutional applications will also be reviewed by the appropriate Council, Board, or other advisory group to the PHS awarding unit whose activities relate to the proposed research training. Institutional applications will be evaluated on the basis of qualifications of participating faculty, the proposed research training objectives and program design, and the previous training record of the research program and its ability to attract high-caliber trainees. The extent of the institutional commitment, the available facilities, the quality of the training environment, and the relationship of the proposed program goals to the needs for research training in specified NIH, ADAMHA, and HRA/DN program areas will be considered. Applications for individual fellowship awards will be evaluated on the basis of the applicant's past academic and research record, the research training proposal, the sponsor's general qualifications, the training environment, publications, references, other relevant information, and the applicant's research goals in terms of the research training priorities specified by the awarding unit. Individual fellowship applications receive the normal initial review and a secondary staff review and are not reviewed by National Advisory Councils or Boards.

4. Notification of Action

The applicant will be notified by letter concerning the final review recommendation. Approximately six to nine months transpire between the initial application and final notification. A Notice of Grant Award will be issued to applicants selected for funding.

5. Period of Support

Institutional grants may be made for competitive segments of up to five years and are renewable. Awards within an approved competitive segment are normally made in 12-month increments with support for additional years dependent upon satisfactory progress and availability of funds. Trainees are customarily appointed for full-time 12-month periods. No trainee may be appointed under an institutional grant for less than nine months except with the prior approval of the awarding unit; and then usually only to complete a planned program of training. An appointment or a reappointment may not exceed 12 months without prior approval by PHS. The amount of the stipend and tuition for each full period of appointment must be obligated from funds available at the time the individual begins his/her training unless other instructions are furnished by PHS.

HRA/DN awards predoctoral individual fellowships for periods up to five years. ADAMHA limits predoctoral fellowships to three years. NIH, ADAMHA, and HRA/DN limit postdoctoral support to three years. The awards are made in 12-month increments.

All trainees and fellows are required to pursue their research training on a full-time basis devoting no less than 40 hours per week as specified by the sponsoring institution in accordance with its own policies.

No individual trainee or fellow may receive more than five years of aggregate NRSA support at the predoctoral level and three years of aggregate NRSA support at the postdoctoral level, including any combination of support from institutional and individual awards. Any exception to this requires a waiver from PHS based on review of justification from the individual and the sponsoring institution. The grounds for approving extensions of support are as follows:

a. Physicians

Individuals requiring additional time to complete training, either as a participant in a combined M.D.-Ph.D. program or physicians, dentists, and veterinarians who are completing postdoctoral research training, may anticipate favorable consideration of a reasonable request for waiver of the time limitation. This action is contingent upon certification of the recipient's good academic standing.

b. Interruptions

Requests for additional time will also be considered if an event unavoidably has altered the planned course of the research training; the interruption has significantly detracted from the nature or quality of the planned research training; and if a short extension would permit completion of the training as planned. Such events include sudden loss of the preceptor's services or an accident, illness, or other personal situation, which prevents a trainee or fellow from pursuing his/her research training in an effective manner for a significant period of time. Requests for extension of support will also be considered if a short additional period would provide the trainee or fellow an opportunity to use an exceptional training resource.

c. Other Exceptions

Requests that do not arise from circumstances considered in 5.a. or 5.b. will be considered if they are accompanied by an exceptionally strong justification.

Requests for extension must be made in writing by the trainee or fellow and addressed to the awarding unit. The trainee's program director, or in the case of fellowship, the sponsor, must endorse the request certifying the need for additional time. The request must include a sound justification and specify the amount of additional time for which approval is sought.

6. Initiation of Support

a. Individual Fellowship

(1) The awarding unit will notify the individual of the intention to make an award and confirm the actual plans for the start of the fellowship support. The Notice of Grant Award will be issued so that the individual may begin the fellowship immediately, or to permit a period of up to 12 months for the individual to finalize arrangements, such as the completion of degree requirements, final coordination with the sponsor, and, if necessary, a move to the sponsoring institution. The fellow must start the period of training under the award by the latest effective date or activation date as shown on the Notice of Grant Award.

The day the fellow begins training, the Activation Notice and the Payback Agreement must be completed and submitted to the awarding unit (see Sections D.1.(a)(1) and (2)). A stipend may not be paid until these forms are submitted and the fellow begins training. If necessary for payroll purposes, the Activation Notice and Payback Agreement may be submitted up to 30 days in advance of the begin date. However, any change in this planned begin date must be reported immediately to the business office and the awarding unit. If an award is conditioned upon the completion of degree requirements, certification of completion by the degree granting institution must be submitted with the Activation Notice.

Subsequent periods of approved fellowship training are consecutive with the first year of support and are usually in 12-month increments. An Activation Notice and Payback Agreement are required at the beginning of each new year of support. If a fellow decides not to activate the award, or to terminate early, he or she should notify the institutional business office and the awarding unit immediately.

(2) Domestic sponsoring institutions receive an award for the stipend and the institutional allowance. The fellow is then paid directly by the domestic institution, which also disburses the institutional allowance.

Fellows training at Federal laboratories are paid directly by the awarding unit, which also reimburses the fellow for appropriate expenditures from the institutional allowance. Fellows training at foreign sites receive direct payment for their stipend from the awarding unit, however, the institutional allowance is awarded to and disbursed by the sponsoring institution. See Exhibit I for a summary of the general steps in the NRSA program (Fellow).

b. Institutional Trainee A Notice of Grant Award is issued to the grantee institution normally with a start date of July 1 and with a budget period of 12 months.

A predoctoral or postdoctoral trainee may be appointed at anytime during the course of the budget period for an appointment period of 12 months.

At the time of each appointment, the training program director must submit a Statement of Appointment and a Payback Agreement to the awarding unit (see Sections D.1.(b)(1) and (2)). The Statement of Appointment includes biographical data on the trainee and the stipend level for the period of training. The stipend is paid by the institution directly to the trainee.

Subsequent appointments are consecutive with the first year of support. A Statement of Appointment and Payback Agreement must be submitted with each reappointment. See Exhibit I for a summary of the general steps in the NRSA program (Trainee).

C. FINANCIAL PROVISIONS

1. Stipends

A stipend is provided as a subsistence allowance for trainees and fellows to help defray living expenses during the research training experience. It is not provided as a condition of employment with either the Federal Government or the institution. Changes in stipend levels are published in the NIH Guide for Grants and Contracts. Stipends must be in accordance with the stipend levels set by this policy. No departure from the standard stipend schedule, as provided from the grant, may be negotiated by the institution with the trainee. Institutions may supplement stipends as necessary from institutional resources; however, no supplementation may be provided from Federal funds unless explicitly authorized under terms of the specific program from which the supplemental funds are derived. (See Sections D.2. and D.3. on Concurrent Benefits, Supplementation and Compensation).

a. Predoctoral individuals The current stipend level for predoctoral individuals at all levels of experience is $5,040 per annum.

b. Postdoctoral The stipend level for the entire first year of support is determined by the number of years of relevant postdoctoral experience at the time of appointment or in the case of an individual fellow, at the time the award is issued. Relevant experience may include research experience (including industrial), teaching assistantship, internship, residency or other time spent in full-time studies in a health related field beyond that of the qualifying doctoral degree. The stipend for each additional year of NRSA support is the next level in the stipend structure and does not change mid-year. Current stipends effective July 1, 1980 for postdoctoral trainees and fellows are as follows:

Years of Relevant Experience	Stipends
0	$13,380
1	14,040
2	14,736
3	15,468
4	16,236
5	17,040
6	17,892
7 or more	18,780

c. Senior Fellows (NIH only) The amount of the stipend to be paid shall be commensurate with the salary or remuneration which the individual receiving the award would have been paid by the institution with which he or she has a permanent affiliation on the date of the fellowship award, but in no case shall the NIH stipend award exceed $30,000. Fringe benefits are not provided with this award. The level of NRSA support will take into account concurrent salary support provided by the institution, other supplementation, and the policy of the sponsoring institution. Senior fellowships are made for full-time research training. Health professionals may utilize some of their time in clinical duties only if it is an integral part of the research training experience.

2. Other Costs

a. Individual Awards

(1) Institutional Allowance An institutional allowance to support the costs of training may be requested and awarded. Based on guidelines effective July 1, 1980, allowances of up to $4000 per year for a predoctoral fellow and $5000 per year for a postdoctoral or senior fellow may be authorized. (NIH makes no individual awards for predoctoral fellows, except for the MARC Program.) An allowance of up to $2000 is available for an individual training at a Federal laboratory. Annual fiscal constraints may modify the maximum levels approved in awards. Changes in allowance levels are published in the *NIH Guide for Grants and Contracts*.

The allowance is intended to defray such expenses for the individual fellow as tuition and fees, research supplies, equipment, travel to scientific meetings, medical insurance, and to otherwise offset, insofar as possible, appropriate administrative costs of graduate training. The $2000 allowance for individuals training at Federal laboratories, which is administered by the PHS awarding unit, is intended to cover the costs of scientific meeting travel, medical insurance, and tuition and fees for specific courses. The following are specific guidelines for the use of the institutional allowance:

(a) A fellow's tuition and fees, and medical insurance are allowable costs only if required of all persons in a similar training status regardless of the source of support. Family medical insurance is not an appropriate charge; however, the individual may elect personally to pay the differential between Self and Family options. Tuition and fees for postdoctoral fellows are limited to those for specific courses required by the training program.

(b) Payment for travel to scientific meetings is appropriate when it is necessary to the individual's training. For fellows at Federal laboratories, reimbursement for travel cost is in accordance with the current government travel regulations prevailing at the Federal laboratory to which the fellow is assigned.

(c) Funds may not be expended to cover the costs of travel between the trainee's place of residence and the domestic training institution, except that the grantee institution may authorize the cost of a one-way travel allowance in an individual case of extreme hardship.

(d) The sponsoring institution authorizes the expenditure of the allowance in behalf of the fellow according to the institutional policy. The institution is entitled to expend up to the full institutional allowance upon official activation of the award. However, if an individual fellow is not in a training status for more than six months or more of the award year, only one-half of that year's allowance may be charged to the grant, the other half must be refunded to the PHS.

(2) Travel to Foreign Training Site The awarding unit may authorize the cost of a single round trip economy or coach ticket to an approved foreign training site. As in the case of all foreign travel, U.S. carriers must be used when available.

(3) Field Research Travel ADAMHA may also provide an additional allowance for field research where a fellow is undertaking a field research project as part of the research training and the annual allowance is not sufficient to cover the costs of such research.

b. Institutional Awards

(1) Institutional Costs Funds are provided to defray the costs of training expenses such as staff salaries, consultant costs, equipment, research supplies, staff travel, and other expenses. Institutional costs of up to $3000 per year per predoctoral trainee and up to $5000 per year per postdoctoral trainee may be awarded based on the requested and approved budget. The current levels are based on the July 1, 1980 guidelines. Annual fiscal constraints may modify the maximum levels approved in grant awards. Changes in allowance levels are published in the *NIH Guide for Grants and Contracts*.

(2) Trainee Tuition and Fees Tuition, fees and medical insurance are allowable trainee costs only if such charges are required of all persons in a similar training status at the institution, without regard to their source of support. Tuition at the postdoctoral level is limited to that required for specific courses in support of the approved training program. The trainee's medical insurance is an allowable cost only if required of all persons in a similar training status regardless of the source of support. Family medical insurance is not an appropriate charge. However, the trainee may elect personally to pay the differential between Self and Family options.

(3) Trainee Travel Costs If requested by the institution, the awarding unit may award grant funds to cover the costs of trainee travel including attendance at scientific meetings which the institution determines to be necessary to the individual's training. Funds may not be expended to cover the costs of travel between the trainee's place of residence and the training institution, except the grantee institution may authorize a one-way travel allowance in an individual case of extreme hardship.

(4) Rebudgeting of Funds PHS policy regarding prior approval and the use of grant funds pertains to NRSA awards. Funds awarded in an institutional grant for trainee costs (stipends, tuition, fees, and medical insurance) may not be used for other purposes except under unusual circumstances and then only with the prior approval of the awarding unit. Rebudgeting into or within the category of trainee costs is allowable without awarding unit prior approval. Trainee travel is not considered a trainee cost for the purpose of rebudgeting.

(5) Expenditure of Funds Expenditure of all training grant funds are those permitted under the Public Health Service Grants Policy Statement and applicable cost principles, unless otherwise indicated in the Notice of Grant Award. A reasonable amount up to that awarded for institutional costs is considered available for expenditure even if the full complement of approved trainee positions is not filled.

(6) Indirect Costs On the institutional training grants, the institution will receive actual indirect costs or 8% of total direct costs (exclusive of tuition, fees and equipment) whichever is less. Applications from State and local government agencies may receive full indirect cost reimbursement.

D. OTHER TERMS AND CONDITIONS

1. Reporting Procedures for Individuals and Institutional Award Recipients

The following documents are critical to the process of establishing the payment of stipends and other costs, as well as the determination of possible payback service.

a. Individual Awards

(1) Activation Notice (Form PHS 416-5, See Exhibit II) Immediately upon the initiation of training the individual completes and signs the Activation Notice, obtains the signature of the designated sponsoring institution officials, and forwards the notice along with the payback agreement to the NIH, ADAMHA, or DN awarding unit. An Activation Notice is enclosed with each Notice of Grant Award.

For fellows whose stipend is paid through the institution, the Activation Notice may be submitted up to 30 days before the individual goes on duty if such is necessary for payroll purposes. However, the institution should not release any money until the individual has actually begun training. Furthermore, if the individual does not begin research training on the day indicated, the institution must notify the PHS awarding unit immediately.

For fellows paid directly by PHS, the forms should not be submitted before he or she actually goes on duty. Stipend checks are issued when both the Activation Notice and the Payback Agreement are received by the awarding unit.

Approved continuation awards must be activated on the day following termination of the previous award period.

(2) Payback Agreement (Form PHS 6031, See Exhibit IV) A National Research Service Award Payback Agreement must be signed by each individual who is to receive an individual fellowship and be submitted to the awarding unit annually with the Activation Notice. This form will be completed beginning with the initial period of support even though the first 12 months may be excluded from the cumulative payback requirement.

(3) Progress Reports Interim progress reports must be submitted with all applications for continuation or renewal support in accordance with the instructions accompanying the application forms. For individual awards the terminal progress report is required as part of the Termination Notice.

(4) Termination Notice (Form PHS 416-7, See Exhibit V) Under an individual award, a Termination Notice form is sent to the fellow by the awarding unit about one month prior to the scheduled termination date; for early terminations the form will be issued immediately upon receipt of information from the awardee or an authorized institution official. This form must be completed and returned to the awarding unit immediately. The lack of timely and accurate information on this form could adversely affect the payback determination.

(5) Financial Status Report An annual or final Financial Status Report is not required on individual awards. In the event of early termination, the stipend must be prorated according to the amount of time spent in training. As mentioned in Section C.2.a.(2), one-half of the allowance must be refunded if the training has been for six months or less.

(6) Changes in the Project Individual awards are made for training at a specific institution under the guidance of a particular sponsor. A transfer to another institution, or a change in sponsor, requires the prior approval of the awarding unit. As a part of that approval process, if a fellow sponsored by a domestic non-Federal institution requests a transfer to another domestic non-Federal institution before the end of the current award year, the initial institution will continue to pay the stipend until the end of the current award year. Disposition of the institutional allowance is negotiable between the two sponsoring institutions.

Any proposed change in the individual's specified area of research training will be reviewed by the awarding unit to assure that the training continues, as required by law, to be in an area of need as specified by the awarding unit.

An interim sponsor must be named by the institution and approved by PHS when the sponsor is going to be absent for a period of more than three months.

b. Institutional Awards

(1) Statement of Appointment (Form PHS 2271, See Exhibit III) The institution must submit this form to the awarding unit at the start of each trainee's appointment or reappointment. No stipend or other allowance may be paid until the appointment form has been submitted along with a signed Payback Agreement. It is important to note that the information on the Statement of Appointment and the Termination Notice is the basis for determination of the length or amount of an individual's payback

requirement. The program director and the institutional financial officials should coordinate the information reported on the Statement of Appointment. It should be treated as a financial document for obligating costs (stipends) which later are reflected as part of the total costs in the Financial Status Report (see Section D.1.b.(6)). A supply of Statement of Appointment forms (PHS 2271) is provided to the program director by the awarding unit.

(2) Payback Agreement (Form PHS 6031, See Exhibit IV) A National Research Service Award Payback Agreement must be signed by each individual who is to receive a stipend through an institutional award. This form and the Statement of Appointment is submitted annually at the time of each appointment. This form will be completed beginning with the initial period of support even though the first 12 months may be excluded from the cumulative payback requirement.

(3) Verification Reports (for NIH only) A computer list identifying trainees for whom a Statement of Appointment of trainee form has been received by NIH will be mailed to program directors 60 days after the budget end date of each institutional grant. The list must be verified by the program director and an appropriate business official and returned to the Trainee Control Unit of the Division of Research Grants within 30 days after receipt.

(4) Progress Reports Interim progress reports must be submitted with all applications for continuation support in accordance with the instructions accompanying the application forms. In addition, a terminal progress report must be submitted to the awarding unit within 90 days after the end of each competing segment of a project period.

(5) Termination Notice (Form PHS 416-7, See Exhibit V) The institution must submit a Termination Notice immediately upon a trainee's termination of support under the grant. The lack of timely and accurate information on this form could adversely affect the payback determination. A supply of Termination Notices will be sent to program directors annually by the awarding unit.

(6) Financial Status Report A Financial Status Report is required for all institutional grants no later than 90 days after the close of each budget period. This report will document the financial status of the grant according to the official accounting records of the grantee institution. Stipends and tuition are obligated for the full 12-month appointment from the budget

period in which the appointment is initiated. Portions of stipends and tuition that extend beyond the budget period are carried as unliquidated obligations. However, the report for the final budget period must have no unliquidated obligations and must indicate the exact balance of unobligated funds.

(7) Changes in the Project Changes in the program objectives as they relate to the area of research training for which the grant was approved require prior approval by the awarding unit. Where absence of the program director is expected to exceed a continuous period of more than three months, plans for the conduct of the program during his or her absence must be approved by the awarding unit. Any proposed change of program director must be requested by the grantee institution and be approved by the awarding unit following review of the nominee's qualifications and re-evaluation of the project in the light of the proposed change. Institutional grants may be transferred from one institution to another only under most unusual circumstances. Such a change will generally be approved only if all of the major benefits attributable to the original grant can be transferred.

c. Interim Revisions

(1) Any changes or corrections involving an appointment under an institutional grant, i.e., name, permanent mailing address, period of training, stipend support, must be reported by the training program director to the awarding unit on an amended PHS-2271 at the time of the change.

(2) Any such changes related to an individual NRSA should be reported immediately by the fellow to the awarding component by letter.

2. Concurrent Benefits

A National Research Service Award may not be held concurrently with another Federally-sponsored fellowship or similar Federal award which provides a stipend or otherwise duplicates provisions of the NRSA. An individual may accept concurrent educational remuneration from the Veterans Administration (e.g., G.I. Bill) and Federal loan funds.

3. Stipend Supplementation - Student Compensation

Trainees and fellows are supported for 12-month full-time training appointments for which they receive stipends to defray their expenses. Stipends may be supplemented by an institution from non-Federal funds without obligation by the fellow or trainee. Institutions can determine what amount of stipend supplementation, if any, will be provided according to their own formally established policies governing stipend support. These policies must be consistently applied regardless of the source of funds. No Federal funds may be used for stipend supplementation unless specifically authorized under the terms of the program from which the funds are derived. An individual may make use of Federal educational loan funds or V.A. benefits when permitted by those programs as described above in Section D.2.

It is recognized that trainees and fellows as students may seek part-time employment coincidental to their training program in order to further offset their expenses. In circumstances of actual employment, the funds provided as compensation (salary/tuition remission) for services rendered, such as, teaching or laboratory assistance are not considered stipend supplementation. Funds characterized as compensation may be paid to fellows and trainees when there is an employer-employee relationship, the payments are for services rendered, and the situation otherwise meets the conditions of the compensation of students as detailed in the PHS Grants Policy Statement. Under these conditions trainees and fellows may be compensated for actual employment on Federal grants, including PHS research grants. However, it is expected that compensation from research grants will occur on a limited part-time basis for employment apart from the normal training activities which require a minimum of 40 hours per week (see Section B.5.).

Under no circumstances may the conditions of stipend supplementation or coincidental employment detract from or prolong the approved training program.

Compensation may not be paid from a research grant which supports the same research that is part of the trainee's planned training experience as approved in the training grant application. Training grant program directors must approve all instances of employment on research grants in order to verify that the circumstances will not detract from or prolong the approved training program.

4. Leave

a. Vacations and holidays Trainees in academic institutions are not entitled to vacations as such. They are entitled to the normal short student holidays observed by their training institution. The time between semesters or academic quarters is to be utilized as an active part of the training period. Trainees in non-academic institutions are entitled to the holiday and vacation schedule applicable to all trainees at the institution. A period of terminal leave (vacation) is not permitted nor may payment from grant funds be made for leave not taken.

b. Other leave Up to 15 days per year of sick leave with pay may be taken without requesting permission from the awarding unit. Additional sick leave or other leaves of absence must have the prior approval of the sponsor or program director and the awarding unit.

5. Termination

The Director of the awarding agency may terminate an individual award or training grant prior to its normal expiration date (1) at the written request of the recipient, or (2) if the Director finds that the recipient has materially failed to comply with the terms and conditions of the award or to carry out the purpose for which it was made. In the event an award is terminated, the Director shall notify the awardee in writing of this determination, the reasons therefore, the effective date, and the right to appeal the decision.

6. Publications

Trainees and fellows are encouraged to submit reports of their findings for publication to the journals of their choice. Responsibility for direction of the project should not be ascribed to NIH, ADAMHA, or HRA/DN. However, awarding unit support must be acknowledged by a footnote in language similar to the following: "This investigation was supported by (Name of Agency), National Research Service Award (number) from the (awarding unit)."

7. Copyright

Except as otherwise provided in the conditions of the award, when publications or similar materials are developed from work supported by the awarding unit the author is free to arrange for copyright without awarding unit approval. Any such copyrighted material shall be subject to a royalty-free nonexclusive and irrevocable license to the Government to reproduce them, translate them, publish them, use and dispose of them, and to authorize others to do so.

8. Disposition of Professional Fees

Fees resulting from clinical practice, professional consultation or other comparable activities performed pursuant to the purpose of the award may not be retained by the awardee. Such fees will be assigned to the sponsoring or grantee institution for disposition in accordance with PHS policy on grant related income, within the established policies of the sponsoring grantee institution.

The term professional fees does not apply to honoraria, and fees for scholarly writing, delivery of occasional outside lectures, and service in an advisory capacity to public or private nonprofit organizations. These fees, if within institutional policy, may be retained by the awardee.

9. Taxability of Stipends

Section 161(b) of the Revenue Act of 1978, as amended, stated that (a) an amount paid to, or on behalf of, an individual from appropriated funds as a National Research Service Award under section 472 of the Public Health Service Act was to be treated as a scholarship or fellowship grant under section 117 of the Internal Revenue Code of 1954 and (b) the provisions of subsection (c) applied to awards made during calendar years 1974 through 1981.

Section 117 is that part of the Internal Revenue Code which applies to the tax treatment of all scholarships and fellowships. In general, it provides that, subject to certain limitations, degree candidates may exclude the full amount of their scholarships or fellowships from their gross income for purposes of taxation, and non-degree candidates may exclude up to $300 a month of such awards for up to 36 months.

The provisions of 161(b) expired December 31, 1981, and so the exemption allowable under Section 117 may no longer pertain to NRSAs. This legislation may be renewed, however implementation is uncertain.

It must be emphasized that the interpretation and implementation of the tax laws are the domain of the Internal Revenue Service and the courts. PHS takes no position on what the status may be for a particular taxpayer, and it does not have the authority to dispense tax advice. Individuals should consult their local IRS office about the applicability of the law to their situations and for information on the proper steps to be taken regarding their tax obligations. The business office of the sponsoring institution will be responsible for the annual preparation and issuance of the IRS Form 1099-MISC, "Statement for Recipients of Miscellaneous Income" for all fellows and trainees paid through the institution. PHS will issue the subject form for all fellows paid directly by them (fellows training at federal or foreign laboratories).

10. Nondiscrimination

Institutions administering National Research Service Awards are subject to (a) the prohibition against discrimination on the basis of race, color, or national origin imposed by Title VI of the Civil Rights Act of 1964 and the implementing DHHS regulations (45 CFR Part 80); (b) the prohibition against discrimination on the basis of sex imposed by Title IX of the Education Amendments of 1972, and in particular, section 901 of such Act and the implementing DHHS regulations (45 CFR 84); (c) the prohibition against discrimination against the handicapped imposed by section 504 of the Rehabilitation Act of 1973, as amended, and the implementing DHHS regulations (45 CFR 86); and (d) the prohibition against age discrimination imposed by the Age Discrimination Act of 1975 (45 CFR 90).

Applicant organizations are required to have appropriate Assurance of Compliance forms, e.g., HEW 441, HEW 641, HEW 639, or any other required assurances on file with the Office for Civil Rights, Office of the Secretary, DHHS, before a grant may be made to that institution.

11. Human Subjects - Animal Welfare - Recombinant DNA

No award may be made unless the sponsoring or grantee institution has complied with the following:

(a) HHS Regulations for the Protection of Human Subjects (45 CFR 46), which require written Assurance of Compliance with the regulations and Certification to HHS of review and approval by an institutional review board for all nonexempt research involving human subjects;

(b) Chapter 1-43 of the HHS Grants Administration Manual (Chapter 1-43 of the PHS Grants Administration Manual) which requires written assurance of compliance with PHS animal welfare policy. (The Office for Protection from Research Risks, NIH, 3A18 Westwood Building, Bethesda, MD, 20205, can be contacted for information and instructions on the requirements for protection of human subjects and animal welfare.)

(c) The current NIH Guidelines for Research Involving Recombinant DNA Molecules. (The Office of Recombinant DNA Activities, NIH, Building 31, Room 4A52, Bethesda, MD 20205, can be contacted for further information.)

E. PAYBACK AND REPORTING REQUIREMENTS FOR RECIPIENTS

1. Background

The National Research Service Award legislation requires recipients of support to pay back the Federal Government by engaging in health related biomedical or behavioral research and/or teaching. The NRSA payback obligation may be satisfied by either serving in a position in which biomedical or behavioral research and/or teaching constitutes more than 20 hours per week or by financially recompensating the Government in an amount of money determined in accordance with a recovery formula specified in the legislation. Payback is required in an amount equal to the total period of support in excess of the initial 12 months of support. This section outlines the payback provisions and procedural requirements necessary for institutions and individuals to comply with the payback obligation.

2. Amount of Payback Service

The amount of required payback service is equal to the total period of support in excess of the initial 12 months of postbaccalaureate support. Once an individual has had 12 months of postbaccalaureate NRSA support, all subsequent NRSA support is subject to payback.

3. Criteria for Acceptable Payback

The NRSA payback obligation may be satisfied by either serving in a full-time position in which health-related research and/or teaching constitutes the primary activity or, if not serving in a full-time position of this kind, engaging in such research and/or teaching in a position(s) for periods that average more than 20 hours per week of a full work year. Full-time credit is given for service meeting this guideline. It is generally expected that any full-time academic appointment in a biomedical or behavioral field would meet the payback requirement. Teaching and research duties include not only time spent in the classroom, laboratory, or research clinic, but also time spent in preparation for those activities. Total employment averaging 20 hours or less a week cannot be counted toward fulfilling the payback obligation.

Payback service must be performed following completion of NRSA training. No amount or type of activity prior to or during the tenure of NRSA support will satisfy the NRSA payback obligation.

a. Research For the purposes of NRSA, research is defined as activity which involves the design of experiments, development of protocols and collection and interpretation of data. Research support functions, such as routine laboratory analyses, managerial and administrative activities, and a technical advisory role on development or marketing of products are not considered to be research.

b. Teaching The range of activities acceptable as teaching will take into account the certifying institution's policy on the definition of teaching responsibilities. Teaching activities will be accepted only if they take place in an organized educational or other instructional environment.

c. Research Setting The research setting may be in the academic, governmental, or commercial sector--domestic or foreign. The academic sector includes universities, professional schools, research institutes, teaching hospitals, colleges, and universities. The source of funds supporting the payback activity is not generally restricted. An individual could be supported by a PHS grant or by a grant or fellowship from another organization. The only restriction on the sources of funds is that a payback activity may not be supported by another NRSA award.

d. Payback Limitations Credit for research and teaching activities undertaken by the recipient after terminating NRSA support, but while still in training status (e.g., activities as graduate student, resident, or clinical fellow), is subject to the following limitations:

(1) Credit for service will be given only in instances where the proposed teaching and/or research activities include responsibilities that distinguish them from activities required of trainees and which require more than 20 hours per week. For graduate students the distinguishing feature may be assignment of responsibility as teaching assistant or laboratory instructor, or responsibility for conduct of research; for residents and clinical fellows the distinguishing feature may be teaching responsibility other than clinical supervision, or responsibility for conduct of research that is not a requirement of residency training.

(2) Without such distinguishing responsibilities, the dissertation research of graduate students or the clinical supervision characteristic of residency or clinical fellowship training are unacceptable as payback service. However, some advanced resident positions in which research and/or teaching is either the primary activity or involves more than 20 hours a week may count toward fulfilling the payback obligation.

4. Alternative Service

Alternative service in lieu of research and teaching was deleted by the Omnibus Budget Reconciliation Act of 1981. Individuals who entered the NRSA program on or after August 13, 1981, the date the Act was signed, are not eligible for alternative service. Individuals who entered the NRSA program before August 13, 1981 are governed by the alternative service provisions in effect when their appointment started. The Secretary, DHHS, must authorize alternative service and make a determination that no suitable research or teaching positions are available to the individual. More information on alternative service is available from the awarding unit.

5. Timing of Service Obligation

An individual must begin to undertake the payback service requirement within two years after the termination date of the individual's NRSA support.

6. Financial Payback

If any individual to whom the requirement for service is applicable fails to undertake or perform such service as required in E.5. above, the United States shall be entitled to recover from the individual the amount determined in accordance with the following formula plus interest:

$$A=\emptyset\left(\frac{t-s}{t}\right)$$

Where "A" is the amount the United States is entitled to recover. "Ø" is the sum of the total amount paid to the individual under his/her National Research Service Award support less the amount paid for the initial twelve months. "t" is the total number of months in the individual's service obligation. "s" is the number of months of the obligation served by the individual. The total paid to the individual (Ø) under institutional grants and individual awards at domestic, non-federal sponsoring institutions is considered to be the stipend only. The total paid an individual under a fellowship award at a foreign sponsoring institution includes the payment for the round trip travel costs. The total paid an individual under a fellowship award at a federal sponsoring institution includes any money expended from the institutional allowance provided for such purposes as medical insurance, travel, tuition and fees.

Interest on the amount begins and is at a rate fixed by the Secretary of the Treasury considering private consumer rates which prevail on the date the determination is made that the NRSA payback requirements will not be fulfilled through service. The amount to be recovered financially shall be paid to the United States within the three-year period following such date.

7. Extension or Waiver of Payback

a. Extension The Secretary, DHHS, may extend the period for undertaking payback service, permit breaks in continuous service, or extend the period for repayment if the Secretary determines:

(1) such an extension or break in service is necessary so the individual may complete his or her research training; or

(2) the individual is unable to complete the requirements within the required period because of a temporary disability; or

(3) completion by the individual of the requirement within the required period would involve substantial hardship to the individual and that failure to extend the period would be against equity and good conscience.

Reasons for an extension or break in service include such things as physicians completing residency training and graduate students completing degree requirements. Requests must be made in writing to the awarding unit, specifying the need for additional time and the length of the required extension.

b. Waiver Where an individual fails to undertake or perform such service requirement the Secretary, DHHS, may waive in whole or in part the obligation of the individual to repay upon determination that compliance by the individual is impossible, or would involve substantial hardship, and enforcement of the obligation to that individual would be against equity and good conscience. Requests for waivers should be made in writing to the awarding unit and explain the need for waiver according to the following criteria.

(1) Compliance by an individual will be deemed impossible if the individual is permanently and totally disabled.

(2) In determining whether compliance would involve substantial hardship to the individual and would be against equity, the Secretary shall take into consideration:

(a) the individual's present financial resources and obligations;

(b) the individual's estimated future financial resources and obligations;

(c) the reasons for the individual's failure to complete the requirements within the prescribed period, such as problems of a personal nature;

(d) the extent to which the individual has engaged in payback activities;

(e) whether the individual has received sufficient training to be qualified to perform such activities; and

(f) the unavailability of employment opportunities appropriate to the individual's education and training.

(3) Any obligation of any individual toward payback will be cancelled upon the death of the individual.

8. Annual Payback Activities Certification (Form PHS 6031-1, See Exhibit VI)

a. Annual Certification Approximately one year after the completion of NRSA support, if an individual has incurred a payback obligation, he or she will receive an Annual Payback Activities Certification (APAC) form. On this form, the individual will report the activity in which he or she was engaged for the preceding 12 months. These forms are to be returned within 30 days of the reporting period end date to:

Trainee and NRSA Control Office
Division of Research Grants
National Institutes of Health
Westwood Building
5333 Westbard Avenue
Bethesda, Maryland 20205

The PHS awarding unit will review the activity and make a decision on its acceptability and inform the former awardee of the decision. This process will continue annually until the individual's total payback obligation is satisfied. Individuals who do not submit an APAC or cannot be located will have their file forwarded to the appropriate agency for financial payback.

b. Change of Address Any change in the mailing address of a NRSA recipient must be reported promptly to the Trainee and NRSA Control Office (see above). This should continue for a minimum period of five years following the completion of support or for such additional time as is required to ensure satisfaction of the payback obligation and to participate in occasional program evaluation.

Request for policy clarification in individual cases

should be addressed to the appropriate PHS awarding unit.

Exhibit I

GENERAL STEPS IN THE NRSA PROGRAM

INSTITUTIONAL (TRAINEE)

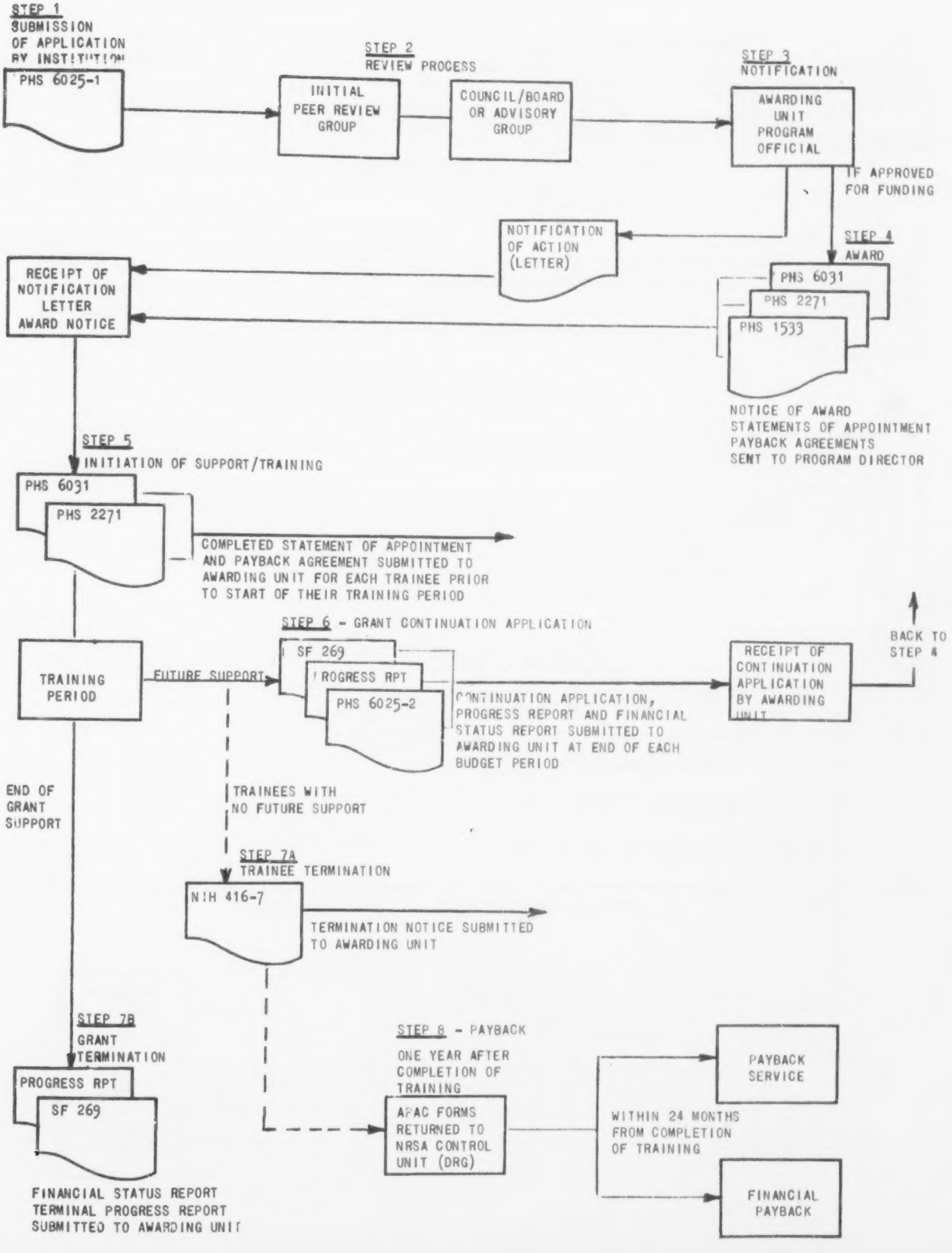
STEP 1
SUBMISSION OF APPLICATION BY INSTITUTION
PHS 6025-1
STEP 2
REVIEW PROCESS
INITIAL PEER REVIEW GROUP
COUNCIL/BOARD OR ADVISORY GROUP
STEP 3
NOTIFICATION
AWARDING UNIT PROGRAM OFFICIAL
IF APPROVED FOR FUNDING
NOTIFICATION OF ACTION (LETTER)
STEP 4
AWARD
PHS 6031
PHS 2271
PHS 1533
NOTICE OF AWARD
STATEMENTS OF APPOINTMENT
PAYBACK AGREEMENTS
SENT TO PROGRAM DIRECTOR
RECEIPT OF NOTIFICATION LETTER AWARD NOTICE
STEP 5
INITIATION OF SUPPORT/TRAINING
PHS 6031
PHS 2271
COMPLETED STATEMENT OF APPOINTMENT AND PAYBACK AGREEMENT SUBMITTED TO AWARDING UNIT FOR EACH TRAINEE PRIOR TO START OF THEIR TRAINING PERIOD
STEP 6 - GRANT CONTINUATION APPLICATION
TRAINING PERIOD
FUTURE SUPPORT
SF 269
PROGRESS RPT
PHS 6025-2
CONTINUATION APPLICATION, PROGRESS REPORT AND FINANCIAL STATUS REPORT SUBMITTED TO AWARDING UNIT AT END OF EACH BUDGET PERIOD
RECEIPT OF CONTINUATION APPLICATION BY AWARDING UNIT
BACK TO STEP 4
END OF GRANT SUPPORT
TRAINEES WITH NO FUTURE SUPPORT
STEP 7A
TRAINEE TERMINATION
NIH 416-7
TERMINATION NOTICE SUBMITTED TO AWARDING UNIT
STEP 7B
GRANT TERMINATION
PROGRESS RPT
SF 269
FINANCIAL STATUS REPORT
TERMINAL PROGRESS REPORT
SUBMITTED TO AWARDING UNIT
STEP 8 - PAYBACK
ONE YEAR AFTER COMPLETION OF TRAINING
APAC FORMS RETURNED TO NRSA CONTROL UNIT (DRG)
WITHIN 24 MONTHS FROM COMPLETION OF TRAINING
PAYBACK SERVICE
FINANCIAL PAYBACK

Exhibit I

GENERAL STEPS IN THE NRSA PROGRAM

INDIVIDUAL (FELLOW)

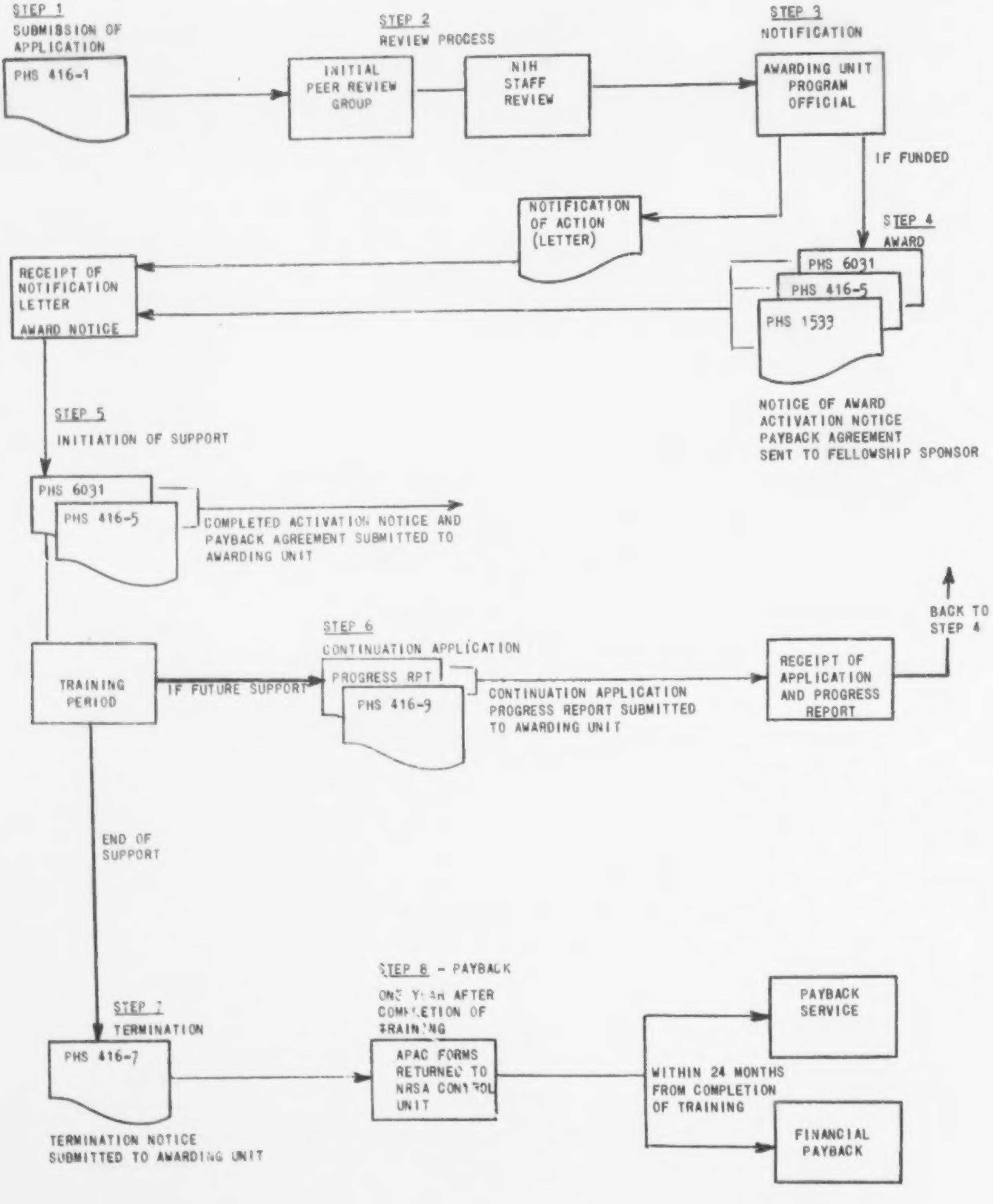
STEP 1
SUBMISSION OF APPLICATION
PHS 416-1
STEP 2
REVIEW PROCESS
INITIAL PEER REVIEW GROUP
NIH STAFF REVIEW
STEP 3
NOTIFICATION
AWARDING UNIT PROGRAM OFFICIAL
IF FUNDED
NOTIFICATION OF ACTION (LETTER)
STEP 4
AWARD
PHS 6031
PHS 416-5
PHS 1533
NOTICE OF AWARD
ACTIVATION NOTICE
PAYBACK AGREEMENT
SENT TO FELLOWSHIP SPONSOR
RECEIPT OF NOTIFICATION LETTER
AWARD NOTICE
STEP 5
INITIATION OF SUPPORT
PHS 6031
PHS 416-5
COMPLETED ACTIVATION NOTICE AND PAYBACK AGREEMENT SUBMITTED TO AWARDING UNIT
TRAINING PERIOD
IF FUTURE SUPPORT
STEP 6
CONTINUATION APPLICATION
PROGRESS RPT
PHS 416-9
CONTINUATION APPLICATION PROGRESS REPORT SUBMITTED TO AWARDING UNIT
RECEIPT OF APPLICATION AND PROGRESS REPORT
BACK TO STEP 4
END OF SUPPORT
STEP 7
TERMINATION
PHS 416-7
TERMINATION NOTICE SUBMITTED TO AWARDING UNIT
STEP 8 - PAYBACK
ONE YEAR AFTER COMPLETION OF TRAINING
APAC FORMS RETURNED TO NRSA CONTROL UNIT
WITHIN 24 MONTHS FROM COMPLETION OF TRAINING
PAYBACK SERVICE
FINANCIAL PAYBACK

Exhibit II

FORM APPROVED
O.M.B. NO. 68-R0299

PLEASE USE TYPEWRITER - RETURN ALL COPIES WHEN MAILING

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE **RESEARCH FELLOWSHIP ACTIVATION NOTICE**	FELLOWSHIP NUMBER DATE FELLOW ENTERED ON DUTY *(Month, day, year)*
NAME OF FELLOW *(Last, first, initial)*	NAME OF SPONSORING INSTITUTION
RETURN TO:	TYPE FULL ADDRESS WHERE CHECKS SHOULD BE MAILED *(For Fellows sponsored by Federal or foreign institutions)*

DO NOT WRITE IN THIS BLOCK *(FOR PHS USE ONLY)*

AWARD PERIOD From: Through:	COMMON ACCOUNTING NUMBER	LIST NUMBER

(FOR DIRECT PAY FELLOWS)

STIPEND
(Monthly) $__________ Total $__________

TRAVEL $__________

OTHER $__________

TOTAL PAYMENT $__________

SPECIAL INSTRUCTIONS

PREPARED BY: __________________

Date: __________________

REQUIRED SIGNATURES

FELLOW	TELEPHONE *(Code, no., and extension)*	DATE
SPONSOR	TELEPHONE *(Code, no., and extension)*	DATE
INSTITUTIONAL BUSINESS OFFICIAL	TELEPHONE *(Code, no., and extension)*	DATE

PHS 416-5
Rev. 7/79

PHS Distribution: Pink copy DRG STATISTICAL COPY

PA: 09-25-0112

Exhibit III

NOTE **See instruction sheet and follow carefully. Complete and submit this form at the time trainee enters training, is reappointed, or the reported appointment is amended. Return Institute/Division copy, green copy, and DRG Statistical copy to the PHS Awarding component. For National Research Service Award (T32) trainees, a signed payback agreement must accompany this form on new and reappointments. PLEASE USE TYPEWRITER.**

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service

STATEMENT OF APPOINTMENT OF TRAINEE

1. Type | Activity | I/D Serial No

2. TYPE OF ACTION (Check one type)
☐ New Appointment (NOT previously supported by this grant)
☐ REAPPOINTMENT (Previously supported by this grant)
☐ AMENDMENT OF ITEMS CHECKED ☐ 3 ☐ 4 ☐ 16 ☐ 18

3. NAME OF TRAINEE (Last, first, initial)

4. **PERMANENT MAILING ADDRESS**

5. SOCIAL SECURITY NO.

6. SEX ☐ F ☐ M

7. Birthdate (Mo.day,yr.)

8. U.S. Citizen or U.S. Noncitizen National ☐ Yes
OR
Permanent Resident of U.S. ☐ Yes
(See instructions)

9. PRIOR NRSA SUPPORT (Individual or Institutional)
☐ Yes ☐ No (If YES, See Instructions)

10. EDUCATION - AFTER HIGH SCHOOL (Include all academic and professional education. For foreign degrees, give U.S. equivalent.)

NAME OF INSTITUTION, DEPARTMENT & LOCATION	Month and Year Attended		Degree(s) Received		MAJOR FIELD	MINOR FIELD
	From	To	Degree	Mo. & Yr.		
(Most recent)						

11. EMPLOYMENT – AFTER COLLEGE (Include military service, internships and residencies)

NAME AND LOCATION OF EMPLOYER	OCCUPATION OR POSITION TITLE	FROM Mo. & Yr.	TO Mo. & Yr.
(Most recent)			

12. **Names of Specialty Boards:**

12A. Seeking Certification For

12B. Certified by (Include date of certification)

13A. Is Trainee Seeking a Degree?
☐ Yes ☐ No

13B. Degree(s) Sought

13C. Month and Year Expected

14A. Discipline, Specialty or Field of Proposed Training

14B. Subdiscipline or Subspecialty of Proposed Training

15. Will this Training be taken in an Institution, School, Department other than that entered in item 19?
☐ Yes ☐ No If "Yes," give complete name and address

16. Period of this Appointment (Month, day, year)
From Thru

17. Approximate percent of trainee's time on this appointment
☐ 100% ☐ 75% ☐ 50% ☐ 25%

18. TRAINING SUPPORT FOR PERIOD OF APPOINTMENT

TYPE	This Grant (omit cents)		Other Sources
	TOTAL	MONTHLY	
Stipend	$	$	$
Tuition & fees	(est)	XXXXXXXXXXX	
Travel (est.)		XXXXXXXXXXX	
TOTAL	$	XXXXXXXXXXX	$

19. This trainee is qualified for the proposed training and is eligible to receive financial support from this grant for the period specified above. A copy of this appointment form will be given to trainee.

Signature of Program Director | Date

Typed Name of Program Director

School | Department

Name and Address of Institution (Street, city, state, zip code)

20. I certify that the statements herein are true and complete to the best of my knowledge, and that I will comply with all applicable Public Health Service terms and conditions governing my appointment. (A willfully false certification is a criminal offense. U.S.Code, Title 18, Section 1001.)

Signature of Trainee | Date

PHS 2271
Rev. 12/80

Form Approved
OMB No. 68-R1162

INSTITUTE / DIVISION COPY

Exhibit IV

NATIONAL RESEARCH SERVICE AWARD
PAYBACK AGREEMENT

This agreement is required under Section 472 of the Public Health Service Act, as amended (42 USC 289l-1), for all individuals who receive a National Research Service Award directly or through an institutional grant.

I. SERVICE REQUIREMENT - In accepting a National Research Service Award, I hereby agree to engage in biomedical or behavioral research and/or teaching within two years after termination of my National Research Service Award. This service shall be on a continuous basis, and shall be for a period equal to my total National Research Service Award support in excess of 12 months.

II. PAYBACK PROVISIONS - I understand that if I fail to undertake or perform such service in accordance with Section I above, the United States will be entitled to recover from me an amount determined in accordance with the following formula:

$$A=\phi\left(\frac{t-s}{t}\right)$$

where "A" is the amount the United States is entitled to recover; "ϕ" is the sum of the total amount paid to me under my National Research Service Award support less the amount paid for the initial 12 months; "t" is the total number of months in my service obligation; and "s" is the number of months of such obligation served.

Except as provided in Section III below, any amount the United States is entitled to recover shall be paid within the three-year period beginning on the date the United States becomes entitled to recover such amount. Interest on the amount begins on the date the United States becomes entitled to recover such amount and is at the rate fixed by the Secretary of the Treasury after taking into consideration private consumer rates prevailing on that date.

III. CONDITIONS FOR BREAK IN SERVICE, WAIVER AND CANCELLATION - I hereby understand that the Secretary of Health and Human Services:

A. May extend the period for undertaking service, permit breaks in service, or extend the period for repayment, if it is determined that:

1. Such an extension or break in service is necessary to complete my research training;

2. Completion would be impossible because of temporary disability; or

3. Completion would involve a substantial hardship and failure to extend such period would be against equity and good conscience;

(over)

B. May waive my obligation if it is determined that:

1. Fulfillment would be impossible because I have been permanently or totally disabled; or

2. Fulfillment would involve a substantial hardship and the enforcement of such obligation would be against equity and good conscience;

C. Will, in the event of my death, cancel any obligation incurred under this payback agreement.

IV. TERMINATION NOTICE - ANNUAL REPORT OF EMPLOYMENT - CHANGE OF ADDRESS AND/OR NAME - I agree to complete and submit a termination notice immediately upon completion of support. I agree to complete and submit an annual post-award report concerning pertinent employment, and agree to keep the Public Health Service advised of any change of address and/or name until such time as my total obligation is fulfilled.

V. PROGRAM EVALUATION - I understand that I may also be contacted from time to time, but no more frequently than once every two years, after the termination of this award to determine how the training obtained has influenced my career. Any information thus obtained would be used only for statistical purposes and would not identify me individually.

VI. CERTIFICATION - In accepting my National Research Service Award, I certify that I will comply with the terms and conditions of this payback agreement.

Signature: ______________________ Date: __________

Support received under PHS Award/Grant No. ______________

Name (Last, First, Middle):

____

(TYPE OR PRINT)

Mailing Address: ______________________

(TYPE OR PRINT)

____

____

____

____

(rev. 11/81)

Exhibit V

FORM APPROVED
O.M.B. NO. 68-R0259

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE

TERMINATION NOTICE
NATIONAL RESEARCH SERVICE AWARD

Please type and submit original and two copies to PHS awarding component. Items 1 through 10 (except 7A) should be completed by Fellow/Trainee; items 7A and 11 by appropriate institution-official. One copy will be returned to the Fellow/Trainee following validation by PHS official.

SEE REVERSE FOR ADDITIONAL INFORMATION

1. NAME OF FELLOW/TRAINEE (Last, first, initial)

2. FELLOWSHIP/TRAINING GRANT NUMBER

3. NAME OF SPONSORING INSTITUTION

4. DEGREE SOUGHT

5. DATE DEGREE RECEIVED OR EXPECTED

6. DATES OF NRSA SUPPORT (Month, day, year) FROM: TO:

7. TOTAL NRSA STIPEND RECEIVED AND NUMBER OF MONTHS SUPPORTED

	AMOUNT OF STIPEND*	NUMBER OF MONTHS
1st Year	$	
2nd Year		
3rd Year		
TOTAL	$	

*See reverse of form.

7A. VERIFICATION OF ITEMS 6 AND 7: Institutions who pay stipends to Fellows and Trainees shall certify the information provided in items 6 and 7 is correct according to institutional records. (Not applicable to Individual Fellows sponsored by Federal or foreign institutions.)

SIGNATURE OF BUSINESS OFFICIAL

DATE

TYPED NAME OF BUSINESS OFFICIAL

TELEPHONE NUMBER

8. Provide short summary of research undertaken during Fellowship/Traineeship tenure and list publications, if any, resulting from the research during this period (do not exceed space below). If Fellowship or Training appointment is being terminated early, please state reason.

9. SIGNATURE OF FELLOW/TRAINEE

DATE

10. MAILING ADDRESS AFTER TERMINATION OF NRSA SUPPORT (Street, city, state, zip code and telephone number)

11. Certification of Sponsor/Program Director: This is to certify that all the information in items 1 through 10 is correct to the best of my knowledge.

SIGNATURE OF SPONSOR/PROGRAM DIRECTOR

DATE

TYPED NAME OF SPONSOR/PROGRAM DIRECTOR

12. THE INFORMATION PROVIDED IN ITEMS 6 AND 7 IS IN AGREEMENT WITH PHS RECORDS.

SIGNATURE OF PHS OFFICIAL

DATE

TYPED NAME AND AWARDING COMPONENT OF PHS OFFICIAL

PHS 416-7
Rev. 9/79

Exhibit VI

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERIVCE

ANNUAL NATIONAL RESEARCH SERVICE AWARD PAYBACK ACTIVITIES CERTIFICATION

(See instructions on reverse of Part 4)

NAME *(Last, first, middle initial)*

PHS FELLOWSHIP OR GRANT NUMBER

ADDRESS *(Correct if address has changed)*

REPORTING PERIOD
FROM:
TO:

RECORD OF PAYBACK OBLIGATION

TOTAL MONTHS OF NRSA SUPPORT	TOTAL MONTHS OF PAYBACK SERVICE PREVIOUSLY CREDITED

TO BE COMPLETED BY FORMER FELLOW OR TRAINEE (Check one of the following)

1. ☐ Have not engaged in payback service during reporting period *(Complete only Section IV)*
2. ☐ Have elected to engage in financial payback *(Complete Section IV)*
3. ☐ Have been engaged in continuous regular payback service during reporting period *(Complete Sections I, III & IV)*
4. ☐ Have been engaged in continuous alternative payback service previously approved by DHEW *(Complate Sections II, III & IV)*

- FOR INFORMATION ONLY -
- NOT TO BE COMPLETED -

SECTION I – CONTINUOUS REGULAR PAYBACK SERVICE

1. Number of months engaged in payback during reporting period ______
2. Position Title ______
3. Nature of Position *(Check one)*
   - ☐ Full-time position with health-related biomedical or behavioral research and/or teaching as primary activity
   - ☐ Other position(s) where health-related biomedical or behavioral research and/or teaching averages more than 20 hours per week of a full work year. (If more than one position is used to fulfill this requirement, specify average number of hours per week for each position.) ______

SECTION II – CONTINUOUS ALTERNATIVE PAYBACK SERVICE

1. Date of approval by Department of Health, Education and Welfare of alternative service ______
2. Number of months engaged in alternative payback during reporting period ______
3. Position Title ______
4. Type of acceptable payback activity (Check one)
   - a. ☐ National Health Service Corps
   - b. ☐ Specialty Practice in Designated Shortage Areas
   - c. ☐ Practice in HMO as Meeting National Research Service Requirements
   - d. ☐ Health Related Service

SECTION III – COMPLETE IF SECTION I OR II IS COMPLETED

NAME OF EMPLOYING ORGANIZATION

ADDRESS OF EMPLOYING ORGANIZATION

Verification of Supervisor *(or, if self-employed, notarized statement)* that employment information reported is accurate

NAME OF SUPERVISOR

TITLE

SIGNATURE

DATE

SECTION IV – CERTIFICATION OF NRSA RECIPIENT

I certify that all of the above statements are true, complete, and correct to the best of my knowledge. *(A willfully false certification is a criminal offense. U.S. Code, Title 18, Sec. 1001.)*

SIGNATURE

DATE

SECTION V – ACCEPTANCE BY PHS OFFICIAL

LEAVE BLANK

NAME AND TITLE OF PHS OFFICIAL

NUMBER OF MONTHS OF ACCEPTABLE PAYBACK SERVICE THIS REPORTING PERIOD

SIGNATURE OF PHS OFFICIAL

DATE

PHS-6031-1
(3-77)

☆U.S. GOVERNMENT PRINTING OFFICE: 1982-361-144:203

11/8

NIH GUIDE for GRANTS and CONTRACTS
DEPARTMENT OF HEALTH AND HUMAN SERVICES

Vol. 11, No. 8, July 16, 1982

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HAVE YOU MOVED?

If your present address differs from that shown on the address label, please send your new address to: Grants and Contract Guide Distribution Center, National Institutes of Health, Room B3BN10, Building 31, Bethesda, Maryland 20205, and attach your address label to your letter. Prompt notice of your change of address will prevent your name from being removed from our mailing list.

The GUIDE is published at irregular intervals to announce scientific initiatives and to provide policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in grants and contracts activities administered by the National Institutes of Health.

Two types of supplements are published by the respective awarding units. Those printed on yellow paper concern contracts: solicitations of sources and announcement of availability of requests for proposals. Those printed on blue paper concern invitations for grant applications in well-defined scientific areas to accomplish specific program purposes.

HE 20. 3008/2:

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NOTICE

MISCONDUCT IN SCIENCE

The NIH currently is reviewing - and when necessary, refining - its procedures related to instances of real or apparent misconduct that occasionally arise in association with its programs. Included under the rubric "misconduct" are (1) mismanagement of funds, (2) fraudulent or markedly irregular practices in carrying out research procedures or handling research results, (3) serious failures to comply with requirements governing the protection of human subjects and the welfare of laboratory animals, and (4) serious failures to comply with any other conditions of an award such as the guidelines for research with recombinant DNA molecules. The purpose of these new procedures is to ensure, as far as possible, that NIH actions with respect to instances of real or apparent misconduct will serve to protect the public interest with due regard for the rights of individuals and institutions accused of wrongdoing. The following topics are being reviewed:

- detection of real or apparent problems
- determination of whether a real problem exists
- imposition of temporary sanctions or other interim actions prior to completion of an investigation
- investigation of problems
- administrative action following completion of an investigation

Specific proposals to improve procedures are being developed by groups of NIH staff, including representatives of all awarding units and investigative offices, as well as representatives from PHS agencies with similar concerns. The process now underway includes opportunities for comments and suggestions from representatives of awardee institutions and advisory groups. This topic was discussed at the meetings of initial review group chairpersons in February and with the Director's Advisory Committee in March of this year. Discussions were also held during the May-June meetings of National Advisory Councils/Boards and will be continued as needed.

It is expected that several products will emerge from these efforts, including more explicit policy and procedural guidance to assist NIH staff in handling allegations of misconduct and dealing with instances of known improprieties in NIH research programs. Also underway are efforts to define more explicitly the responsibilities of awardee institutions to protect the integrity of federal funds, and the rights of participants in research (including human and animal subjects).

NIH welcomes comments and suggestions from the research community, particularly regarding the relationship of NIH procedures to institutional practices and individual investigators. Among the policy issues being considered are the following:

1. How can the NIH most appropriately work to ensure that its staff and awardees are highly sensitive to - and take necessary action in response to - instances of real or apparent misconduct in association with NIH programs?

2. How can the NIH best assess and promote compliance with the conditions of its awards?

3. What are the specific reporting responsibilities of awardee institutions when

misconduct involving an NIH award is known or suspected?

4. What sanctions are most appropriate for various types of misconduct, and how should they be imposed?

Please address any comments or suggestions to:

Dr. William F. Raub
Associate Director for Extramural
Research and Training
National Institutes of Health
Building 1 - Room 107
Bethesda, Maryland 20205

NOTICE

HUMAN SUBJECTS IN RESEARCH PROPOSALS

DIVISION OF RESEARCH GRANTS

Applications submitted to the Division of Research Grants, National Institutes of Health (NIH), which involve human subjects are considered incomplete for initial review without an appropriately completed form HHS 596 (certification/assurance/declaration). It is requested that this form be submitted with the application, but if extenuating circumstances require a delayed submission, applicants should forward the form to the assigned review committee as designated on the post card advising applicants of the assignment of the application. Do not forward to other units of the NIH.

In addition, applications are considered incomplete without the detailed information requested under the section entitled "Research Plan" in the instructions having to do with human subjects.

NIH has no obligation either to accept or to review applications which are considered incomplete. On this basis, applicants are urged to give careful attention to the instructions for use of the "398 kit" to prevent either a return of the application or a deferral in the review.

NOTICE

Enforcement of Page Limitations on Grant Applications

The PHS 398 grant application kit has specific instructions on page limitations for certain parts of an application. The biographical sketch is limited to two pages. In the Research Plan, the "Specific Aims" section is not to exceed one page, the "Significance" section is not to exceed three pages, and the "Progress Report/Preliminary Studies" section is not to exceed eight pages (excluding the lists of professional personnel and publications and the appendix).

Over the past two years, the NIH has given the scientific community an opportunity to become accustomed to these page limitations, but the increasing workload now necessitates a firm stance. Starting with the October 1, 1982 receipt date, applications that exceed the above page limitations without the required brief explanation will be returned.

Please Conserve PHS 398 Forms

Each year the NIH distributes about 100,000 PHS 398 grant application kits, but only about 27,000 of these are returned as submitted applications. We don't know what happens to the other kits. We do know that each kit is expensive to print and mail, and that any funds saved by not wasting applications could be used elsewhere in the NIH system. In order to conserve forms and reduce costs, please follow these guidelines:

For applicant organizations:

- Be sure the staff in your application control office maintain a tighter control over the distribution of the application kits.

For investigators:

- If you have extra PHS 398 grant application kits, don't save them or throw them away. Give them to colleagues to use or return them to your institution's application control office.
- When you need an application form, don't automatically phone the NIH. Check wih your institution's application control office, for these offices have been sent copies of the PHS 398 kits in bulk for your use.

NOTICE

NOTIFICATION OF CHANGE IN LEVEL OF EFFORT OF PRINCIPAL INVESTIGATOR OF NIH OR ADAMHA SUPPORTED GRANTS

Principal Investigators and grantee institutions are reminded that it is the responsibility of both the Principal Investigator and the institution to keep the awarding unit fully informed of all changes that significantly affect the performance of grant-supported research, or create the presumption of such effect. A grant is awarded on the basis of certain commitments by the Principal Investigator and the applicant institution, as described in the application for support. When these commitments change, the awarding unit needs to be informed.

The current "biological revolution" with its attendant commercial interest in biological research has resulted in new relationships between universities and industry and between individual investigators and industry. As these relationships develop, there may be an impact on a particular investigator's research supported by NIH or ADAMHA.

The following are examples of the kinds of situations which can be occasioned by a shifting relationship with industry and which should be brought to the attention of the awarding unit:

1. Significant change in effort devoted to a grant by a Principal Investigator, including absence of a Principal Investigator for major portions of time, even if any one period of absence does not extend beyond three months.
2. Change in the employment status of a Principal Investigator such as leave without pay, or conversion from full-time to part-time employment.
3. Significant change in location of the facilities where the research will be conducted such that the conduct of the research might be affected.
4. Wide geographic separation of Principal Investigator's main locus of activity from the site where grant-supported research is to be conducted.
5. Major involvement of a Principal Investigator with a profit-making organization (other than the usual one-day-a-week consulting arrangements).

NOTICE

MEETING ON CLINICAL TRIAL OF BLOOD GLUCOSE CONTROL AND EARLY VASCULAR COMPLICATIONS OF INSULIN DEPENDENT DIABETES

The National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases, NIH, is planning a meeting to explore private sector interests in the recently initiated, federally-supported multicenter clinical trial to assess the relationship between blood glucose control and development of the early vascular complications of insulin-dependent diabetes. The objective of this meeting will be to describe the study protocol and to discuss the purpose and scope of the trial. In addition to NIADDK staff members, the Chairman of the Steering Committee will be present to represent the participating investigators. Time will be available for questions and discussion.

The meeting will be held on July 28, 1982, at the NIH in Bethesda, Maryland. The NIADDK is seeking to identify parties interested in attending this meeting who have not already learned of the meeting through other sources. Questions should be directed to:

Carolyn Siebert, MPH
Clinical Trials Coordinator
Division of Diabetes, Endocrinology,
and Metabolic Diseases
National Institute of Arthritis, Diabetes,
and Digestive and Kidney Diseases
National Institutes of Health
Westwood Building - Room 607
Bethesda, Maryland 20205

Telephone: (301) 496-7645

DECREASE IN PRICE OF AGED FISCHER 344 RATS

NATIONAL INSTITUTE ON AGING

Investigators currently using Fischer 344 rats from the National Institute on Aging (NIA) contract-supported colony are hereby notified that a decrease in the price of F344 rats will become effective July 1, 1982. Investigators on new and renewal applications should use the new cost figures in estimating cost needs on grant applications.

In order to regain part of the cost of the contract, users are currently being charged a price equal to $3.44 for virgin male or female rats and $4.84 for retired breeder rats, plus the product of a monthly maintenance charge ($3.64) and the number of months the rats reside in the colony (age in months - 1 for virgins, age in months - 9 for retired breeders).

Effective July 1, 1982, the acquisition costs will increase to $3.82 for virgin F344's and to $5.39 for retired breeders. The monthly maintenance charge will decrease to $2.40. Thus a 20 month old virgin F344 rat will cost $49.42 and a 20 month old retired breeder F344 will cost $31.79.

The acquisition costs are expected to remain at $3.82 and $5.39 through May 1985. Monthly maintenance charges will increase to $2.80 on June 1, 1983 and to $3.00 on June 1, 1984.

For additional information about prices, availability, or colony characteristics please contact:

Dr. Richard L. Sprott
or
Mrs. Jane Soban
Animal Models Program
National Institute on Aging
National Institutes of Health
Building 31 - Room 5C19
Bethesda, Maryland 20205

NOTICE

NONHUMAN PRIMATES AVAILABLE

The National Institutes of Health (NIH) is reducing its colony inventory of Macaca mulatta (rhesus) monkeys. All requests should be in letter form and include the title or a brief description of the project, as well as specifications for the animals (number, age, sex and other special characteristics). Prices range from $750 - $1,200 each, and includes shipping within the continental United States. Prices are negotiable for groups of 50 or more. Availability is subject to prior sale. Commercial and foreign inquiries are invited. Contact:

Dr. Carl E. Miller
National Institutes of Health
Building 31 - Room 5B59
Bethesda, Maryland 20205

Telephone: (301) 496-5175

The following animals are available.

Year of Birth	Number Female	 Male
1982	over 100	over 100
1981	134	80
1980	116	14
1979	78	9
1978	25	2
1977	14	9
1976	0	4
1975	15	2
1974	43	5
1973	141	10
1972	186	7

1971	135	15
1970	48	9
1969	8	17
1968 and earlier	25	30

REQUEST FOR RESEARCH GRANT APPLICATIONS:

RFA-NIH-NIDR-NCP-82-2

FLUORIDE AND THE PREVENTION OF ROOT SURFACE CARIES

NATIONAL INSTITUTE OF DENTAL RESEARCH

Application Receipt Date: October 15, 1982

The National Caries Program (NCP) of the National Institute of Dental Research (NIDR) invites research applications for support of studies to investigate the effects of fluoride in the prevention of root surface caries.

Most of the research into the epidemiology, etiology, prevention and treatment of caries has focused on coronal lesions. Very little is known about the root caries process and factors which may prevent or inhibit the destruction of root surfaces. Epidemiologic surveys have shown that the incidence and prevalence of root surface caries is increasing in the U.S. population and that it is becoming a serious public health problem. The etiology of root caries is not fully understood; factors such as diet, salivary properties and rate of flow and the bacterial flora in the mouth are believed to play an important role in the disease process. Root caries is generally associated with gingival recession and advancing age.

Fluoride is an effective agent in the control and prevention of coronal decay. Clinical trials with school-aged children have shown that when fluoride is administered systemically or topically, the incidence of coronal decay is markedly reduced. In addition, life-long adult residents in communities with fluoridated water systems experience fewer carious lesions than those living in non-fluoridated areas. Evidence suggests that fluoride may also be effective against root surface decay. Studies, however, need to be undertaken to establish the effects of fluoride on cementum and its interactions with bacteria believed to be responsible for the destruction of cemental tissue.

I. BACKGROUND INFORMATION

The extent of the population affected with root surface lesions has not been established. However, epidemiologic surveys have shown that it presents a significant health problem in the United States. A study of elderly residents in a hospital for the chronically ill showed that almost 75 percent were affected. Studies on two younger populations, aged 30 to 59 years, consisting of military personnel and their dependents and patients in a Veterans Administration Hospital

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This program is described in the Catalog of Federal Domestic Assistance, Caries Research, 13.840. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulation 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to requirements of OMB circular A-95 or Health Systems Agency review.

showed that about half of the subjects had root surface lesions. An examination of a civilian population between the ages of 18 and 82 years showed that a similar percentage were affected.

Dissolution of both enamel and cementum is accomplished by bacterial acids produced from fermentable carbohydrates. Because of the different caries sites, it has been suggested that there is a unique bacterial flora responsible for each type of caries. However, while certain bacteria have consistently been identified in the progression of coronal caries, there is no clear indication that a unique bacterial flora exists in the case of root caries. Furthermore, bacteria present in enamel caries may also be found in cemental lesions.

Studies have shown that fluoride is an effective agent in the prevention of enamel caries. There is also some evidence that fluoridation of drinking water may reduce the incidence of cemental surface lesions. A comparison of lifelong residents in fluoridated and nonfluoridated communities showed that the percentage of subjects with root surface caries was lower in the fluoridated community.

The cariostatic mechanism of action of fluoride is generally thought to be twofold: (1) an inhibition of the bacterial production of acid; and (2) an increased resistance of enamel to attack and stimulate remineralization of early lesions.

The antibacterial effect of fluoride is related to a number of cellular reactions, not all of which are currently understood. It has been established that fluoride has the ability to bind with components of a number of bacteria found in coronal and root surface plaque and that it interferes with certain metabolic processes within the bacterial cell. For example, studies which have examined the effect of fluoride on streptococci have found that it acts as an inhibitor of enzymes, such as enolase and phosphoglucomutase, which are involved in glycolysis and acid production. Inhibition of the enzyme enolase may also reduce the ability of the cell to transport sucrose into the cell and to synthesize peptidoglycan, a structural component of the bacterial cell wall. Some evidence is available which shows that fluoride may reduce the ability of bacteria to survive in an acidic environment. It is suspected that fluoride may increase the permeability of the cell membrane to acid, decreasing the cytoplasmic pH and reducing the glycolytic activity of the bacteria.

Fluoride affects the crystalline structure of enamel and makes it more resistant to decay. It has also been observed that fluoride promotes the remineralization of partially demineralized enamel and may stimulate repair of incipient carious lesions. Hydroxyapatite, the major inorganic material of enamel, is converted into fluorapatite, which has a lower solubility rate in the presence of acid. Cementum also has been shown to contain hydroxyapatite. Furthermore, it appears that the caries process affects cementum and enamel in a similar manner in that the subsurface is decalcified before the surface layer.

On the basis of what is known about the effectiveness of fluoride in preventing enamel surface lesions, the variety of oral pathogens sensitive to fluoride, the histological and environmental similarities of enamel and cementum as well as the apparent similarities in the caries process in both tissues, it seems reasonable to presume that the preventive aspects of fluoride on enamel will also apply to cementum.

The increasing life span of the U.S. population coupled with the decreasing prevalence of coronal caries will result in a significant increase in the number of root surfaces at risk to decay, making the problem an urgent one at this time. Therefore, it is proposed that the effect of fluoride on cementum and on the bacteria associated with cemental lesions be investigated.

Individual research grant applications are invited for research on this topic. Initially, there will be a single competition with an application receipt date of October 15, 1982; this RFA may be re-issued at a later date.

II. RESEARCH GOALS AND SCOPE

The purpose of this RFA is to solicit high quality research grant applications that would contribute to the understanding of the effect of fluoride on the mineralization, demineralization and remineralization of artificially or naturally induced incipient lesions on root surfaces and elucidate the anticariogenic effects of fluoride on the bacteria associated with this process.

The choice of research objectives, identification of specific aims, development of appropriate protocols and methodologies, and the procedures for analysis and interpretation of data are left to the investigator's initiative. However, once an award is made under this program, any substantial modification of the research originally proposed must be mutually agreed upon by the investigator and the NCP.

III. MECHANISM OF SUPPORT

The support for this program will be the traditional grant-in-aid. It is anticipated that two or three awards will be made, if a sufficient number of high quality applications is received. Although funds have been allocated for this program in the NCP financial plans for fiscal years 1983 through 1985, award of grants resulting from this RFA is contingent upon receipt of appropriated funds for this purpose. Requests should be restricted to three years of support. Starting dates as early as July 1, 1983 may be requested. Funding beyond the first year of the grant will be contingent upon satisfactory progress during the preceding year. All policies and requirements which govern the research grant programs of the PHS, including cost sharing, will apply to grants made as a result of responses to this invitation.

IV. METHODS AND CRITERIA FOR REVIEW

Applications in response to this invitation will be reviewed in competition with each other. The initial review of the applications for scientific an technical merit will be by a special study section of the Division of Research Grants (DRG); secondary review will be by the National Advisory Dental Research Council in May 1983. Applicants will be informed of the outcome of the review shortly thereafter. The earliest possible beginning date will be July 1, 1983.

Questions concerning this RFA and other grant-related activities of the NCP should be addressed to:

John D. Townsley, Ph.D.
Chief
or
Anna M. Barish
Health Scientist Administrator
Caries Research Grants and Contracts Branch
National Caries Program
National Institute of Dental Research
Westwood Building - Room 522
5333 Westbard Avenue
Bethesda, Maryland 20205

Telephone: (301) 496-7884

Applications must be responsive to the objectives of this RFA. Applications judged nonresponsive by the DRG and the NIDR will be processed as regular grant applications, as will applications received after October 15, 1982. The DRG will not accept an application in response to this announcement that is the same as one concurrently being considered by any other NIH awarding unit.

The factors to be considered in evaluating each application will be: (a) the importance of the research problem and the information sought; (b) the adequacy of the experimental design; (c) the feasibility and promise of the methods proposed; (d) the novelty or originality of the application; (e) the training, experience and research competence of potential of the investigator(s); (f) the suitability of the facilities, including the availability of any special resources required; and (g) the appropriateness of the requested budget relative to the work proposed.

Applications should be prepared on form PHS 398, the application form for the traditional research grant, which can be obtained from the DRG, NIH, or from the Institution's application control office. The first (face) page of the application and the outside of the mailing package should be labeled "RESPONSE TO RFA NIH-NIDR-NCP-82-2 Fluoride and Root Surface Caries." The conventional presentation in format and detail for regular research grant applications should be followed and the points identified under the "Review Criteria" must be fulfilled.

The receipt date, for an original and six copies of the completed application is on or before October 15, 1982. Applications should be sent to:

Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205

ANNOUNCEMENT

PULMONARY ACADEMIC AWARD

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Application Receipt Date: November 1, 1982
Letter of Intent: September 1, 1982

The Division of Lung Diseases, National Heart, Lung, and Blood Institute invites national competition for Pulmonary Academic Awards, which have the dual purpose of improving the quality of pulmonary curricula and of fostering research and careers in the respiratory field. Each school of medicine or osteopathy in the United States or its possessions and territories is eligible for such an award. (Awards are limited to one for each eligible school, for a project period up to five years.)

The Division initiated the Pulmonary Academic Award Program to provide a stimulus for development of a pulmonary curriculum in those schools that do not have one and to strengthen and improve the pulmonary curriculum in those schools that do. Awards provide support to individual faculty members for their educational development and for implementation of the pulmonary curriculum. This announcement is expected to be the final invitation to eligible schools to compete for a Pulmonary Academic Award.

This award is intended to:

- encourage development of a quality pulmonary curriculum that will attract outstanding students to pulmonary research and medical practice;
- ensure superior learning opportunities in pulmonary medicine;
- develop promising young faculty whose interest and training are in pulmonary medicine;
- develop superior faculty who have a major commitment to, and possess educational skills for, teaching pulmonary medicine;
- facilitate interchange of educational ideas and methods among awardees and institutions; and
- develop at the grantee institution the ability to strengthen continuously the improved pulmonary curriculum, with local funds, subsequent to the award.

I. CRITERIA FOR THE AWARD

Competitive review for a Pulmonary Academic Award will include assessment of both the sponsoring institution and the proposed awardee. The institution must propose a candidate with competence in pulmonary medicine and a major career interest in improving educational programs. Plans must be presented which will indicate the development or improvement of the pulmonary educational program.

The awardee must be provided with time to acquire the educational skills necessary for personal development as a teacher and for the development of the pulmonary curriculum. Facilities for rigorous pulmonary research and quality patient care must be available.

The candidate must hold an academic appointment at the sponsoring institution at the time of application and have sufficient research training or clinical experience in pulmonary disease to be able to develop and implement a high quality curriculum within the institution. Plans for evaluating the outcome of this effort must be presented. If the candidate's background requires further educational development, the plans to acquire this additional training should be described. Relevent training in epidemiology, clinical trials, behavioral science or other areas could be advantageous in the broader role of the candidate in stimulating an understanding of pulmonary diseases among other peer health professionals in the institution.

II. PROVISIONS OF THE AWARD

Subject to the availability of funds, the non-renewable Pulmonary Academic Award will include funds for the awardee's salary up to $30,000, fringe benefits, curriculum development and actual indirect costs not to exceed 8% of total allowable direct costs.

The proportion of the applicants total salary which is requested from this grant must be commensurate with the time or effort (at least 50%) to be devoted to the Pulmonary Academic Award. The total salary on which it is based must be consistent both with the established salary structure at the institution and with salaries actually provided by the institution from its own funds to other staff members of equivalent qualifications, rank and responsibilities in the department concerned. If full-time salaries are not currently paid to comparable staff members, the proposed salary must be appropriately related to the existing part-time salary structure.

The Awardee may serve as a principal or participating investigator on an NIH-supported grant or contract and may draw salary from it (not to exceed 50%).

III. REVIEW OF APPLICATION

Applications for Pulmonary Academic Awards will be appraised in terms of criteria outlined for the institution and the Awardee in CRITERIA FOR THE AWARD.

The review will include an assessment of the written proposal and will require an interview with the prospective Awardee in Bethesda, Maryland. (Travel expenses for this interview must be paid by the applicant institution). The initial review group will recommend applicants for consideration to the National Heart, Lung, and Blood Advisory Council.

IV. METHODS OF APPLYING

Each prospective applicant should forward a brief letter of intent not later than September 1, 1982, to:

Carol H. Letendre, Ph.D.
Contracts, Clinical Trials, and Training Section
Review Branch, Division of Extramural Affairs
National Heart, Lung, and Blood Institute
Westwood Building - Room 548
Bethesda, Maryland 20205

The Institute requests such letters only to have some idea of the number of applications that may be expected and to start planning for their review.

Application forms (PHS 398) may be obtained from the administrative office of the applicant institution or from the Division of Research Grants, NIH.

V. DEADLINE FOR RECEIPT OF APPLICATIONS

Application Receipt	Council Review	Start Date
November 1, 1982	May, 1983	July 1, 1983

VI. FOR ADDITIONAL INFORMATION

Prospective applicants are encouraged to review the Pulmonary Academic Award Announcement dated June, 1982, which will detail the eligibility requirements and applications procedures. Requests for copies of this announcement and questions related to the Pulmonary Academic Award should be directed to:

Robert M. Conant, Ph.D.
Chief, Prevention, Education, and
Manpower Branch
Division of Lung Diseases
National Heart, Lung, and Blood Institute
Westwood Building - Room 6A12
Bethesda, Maryland 20205

Telephone: (301) 496-7668

REQUEST FOR RESEARCH GRANT APPLICATION:

RFA NIH-NCI-DRCCA-82-10

COMMUNITY CLINICAL ONCOLOGY PROGRAM

NATIONAL CANCER INSTITUTE

Application Receipt Date: November 9, 1982

I. PURPOSE

The Director of the National Cancer Institute (NCI) is interested in establishing a large scale cancer control effort which involves practicing community oncologists in the NCI clinical trials programs. The purpose of the program is to utilize as a resource the increasing number of highly trained oncologic specialists who have entered community practice in recent years. Combining the expertise of community physicians with ongoing clinical research projects will result in a dynamic development and exchange of the newest clinical treatment research findings at the community level. The Community Clinical Oncology Program (CCOP) should: (1) provide adequate support for expanding the clinical research effort in the community setting; (2) involve primary care physicians early in the course of clinical treatment research to provide the benefits of clinical investigation to communities; (3) establish a base for an extension of other cancer control efforts in the areas of prevention, early detection, rehabilitation, and supportive care; and (4) examine selected issues in CCOP performance (e.g., patient accrual and evaluability) and the diffusion of innovative information.

II. BACKGROUND AND PROGRAM PLANNING

The Director of the NCI first expressed the intention to develop the Community Clinical Oncology Program in March 1981. In response to the NCI interest, the Association of Community Cancer Centers established a Committee on Clinical Research. Recommendations with extensive documentation from a series of deliberations by the membership, consisting of 55 health professionals representing communities in 20 states, were presented to NCI.

In July 1981, the Board of Scientific Counselors of the Division of Resources, Centers, and Community Activities (DRCCA) formed a Subcommittee on Community Oncology and Technology Transfer which included academic and community oncologists, cancer center directors and cooperative group chairmen. A position paper developed by this subcommittee was presented to the DRCCA Board of Scientific Counselors, which gave concept approval for the CCOP in October

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This program is described in the Catalog of Federal Domestic Assistance No. 13.399, Cancer Control. Awards will be made under the authority of the Public Health Service Act, Title IV, Section 403 (Public Law 78-410, as amended; 42 USC 284) and administered under PHS grant policies and Federal regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

1981. There has been a broad and extensive involvement of the potential CCOP participants in the development of this new cancer control effort after concept approval. Following the initial developmental activities from January through June 1982, the NCI staff conducted CCOP regional workshops in a number of areas (e.g., California, Texas, New Jersey, Louisiana, Florida, Georgia, Illinois, Massachusetts, Missouri, Virginia, and Washington, D.C.). NCI staff also made presentations in conjunction with the professional meetings of organizations such as the Association of American Cancer Institutes, National Surgical Adjuvant Breast Project, North Central Oncology Group, Eastern Cooperative Oncology Group, and American Society of Clinical Oncology. During this time information was exchanged informally by NCI staff and community participants through individual telephone inquiries and written commentaries. As a result of this vast external informational input, many problem areas have been resolved.

The CCOP initiative is intended to meet the needs of cancer patients by utilizing the trained specialists now practicing in community hospitals and clinics and establish a system of community clinical oncology programs which will participate in clinical research trials. Over 80 percent of patients with cancer are treated in the community with only a small number entering clinical trials. The Division of Cancer Treatment (DCT) of NCI supports a national clinical trials program largely through academic centers. These have included (1) multimodal national and regional cooperative groups, (2) groups in which the investigators have a particular expertise (such as pediatricians), (3) groups that are designed to deal primarily with high technology single modality studies and (4) groups that are specifically disease-oriented. Additional large cancer centers are involved in implementation of local clinical research protocols.

Over the past decade, increasing numbers of highly trained clinical cancer specialists, experienced in clinical research and protocol care, have been entering private practice in the community. Experience within several Cooperative Groups has indicated that physicians caring for cancer patients in the community can maintain high quality clinical research activities similar to that of the academic centers. Evidence exists that new technology can be transferred effectively by having community physicians participate in clinical research activities.

The CCOP will be developed and supported by the Division of Resources, Centers and Community Activities (DRCCA), National Cancer Institute. Participating community programs will be required to enter or refer into NCI-approved clinical trials, designated as high priority by a research base with which the CCOP is affiliated. These research bases may be national or regional multi-disease cooperative groups, specialized cooperative groups or cancer centers currently participating in NCI approved clinical research protocols. Participants are encouraged to enter patients with early stage disease with common cancers and to enter or refer, if appropriate, patients with uncommon cancers.

Patient entry onto clinical trials will be done through collaboration with a maximum of (1) two primary multi-disease research bases (with two, only one may be a cooperative group) having a spectrum of clinical trial protocols available and (2) a maximum of three specialty research bases. Participation with specialty or multi-disease research bases will be considered equal and a CCOP may choose only one of either or a maximum of five when combined affiliations occur. Eligible patients in a single disease category should be allocated to one protocol in the case where multiple affiliations have resulted in overlapping protocols.

The diffusion hypothesis will be tested during the course of the program. A separate CCOP evaluation is planned to test this hypothesis. According to this hypothesis, it is anticipated that participation of some patients in research will beneficially influence those patients not participating in research protocols. Information diffusion in future cancer control programs of the NCI will similarly be tested.

III. OBJECTIVES OF THE COMMUNITY CLINICAL ONCOLOGY PROGRAM

The CCOP initiative is designed:

A. To bring the advantages of clinical research to cancer patients in their own communities, by having practicing doctors and their patients participate in clinical treatment research protocols, and thus foster an exchange between clinical research and cancer control.

B. To reduce national mortality by speeding the transfer of newly developed cancer treatment technology to widespread community application.

C. To provide a basis for involving a wider segment of the community in cancer control activities and investigate the diffusion of cancer therapy advances in community medical practices. The diffusion hypothesis presumes that introduction of quality-controlled clinical research trials in the community will also benefit those patients not treated as part of this protocol.

D. To develop programs to serve as part of a broadly based nationwide resource for quality-controlled distribution of increasing numbers of experimental anti-cancer agents.

E. To facilitate wider community participation in future cancer control and prevention research activities planned by NCI.

IV. CRITICAL ELEMENTS FOR A CCOP

A. The CCOP may be a single clinic, a group of practicing physicians, a single hospital, or a consortium of physicians and/or clinics and/or hospitals.

NCI recognized comprehensive and clinical cancer centers (holding CORE grants) are not eligible. A University hospital which is the major teaching institution for that university will not be eligible. University hospitals and Veterans Administration hospitals may participate as a non-dominant member of a consortium led by a community institution. University hospitals participating as Division of Cancer Treatment funded Cooperative Group members will not be eligible. Unfunded, non-university group members will be eligible. Those institutions that currently participate as part of the Division of Resources, Centers, and Community Activities funded Cooperative Group Outreach Program or Cancer Centers Outreach Program will be eligible. Cooperative Group Outreach Program support will be terminated for successful CCOP applicants. This funding will revert to the National Cancer Institute Cancer Control Program.

B. Each CCOP must have a demonstrated potential and stated commitment to contribute a minimum of 50 evaluable patients per year to approved clinical research protocols active in the center or group with which the community center is affiliated. Although the CCOP is most appropriate for adult patients, for pediatric CCOPs, the 50 patient minimal requirement will be reduced for those applicants able to place a majority of their eligible patients on protocol. The written affiliation agreements between the CCOP and its research bases will specify the priority protocols which can meet this obligation. As one measure of performance, it is expected that 10 percent or more of eligible patients in suitable disease categories available for study to physicians listed as participating in a CCOP application will be placed on protocols. The mix of cancer patients to meet the reporting requirement will be negotiated in advance with the research base. Patients transferred from the community to any NCI supported clinical research program in order to receive protocol treatment, will be credited to the CCOP. Referrals to centers for NCI supported protocol treatment will result in a credit to the referring CCOP of 1.25 per patient toward the minimum patient requirement.

C. Each CCOP is expected to have a committed multidisciplinary professional team appropriate for their expected protocol participation. This may include surgeons, radiation oncologists, medical oncologists, pathologists, oncology nurses, and psychiatrists. Administrative and data management personnel will be necessary. Other appropriate disciplines may be added (e.g., gynecologic oncologists, pediatric oncologists). One of this group will serve as principal investigator. An associate investigator should be named to assure continuity in the event of departure of the principal investigator.

D. Each CCOP must delineate its patient referral area. Consideration will be given to demographic and geographic distribution of CCOPs in the final selection process. Multiple CCOPs competing for the same patient population will be considered but may not be awarded unless warranted by the population density. Individual institutions or consortia may apply but a single administrative focus should be designated.

E. Each CCOP must provide evidence that an affiliation has been established with a nationally recognized clinical cancer research base (e.g., clinical or comprehensive cancer center, national or regional cooperative group). A list of research base options is available upon request (see Section XII). Multiple affiliations are permitted provided they are not conflicting. These affiliations must exist in the form of a written agreement between the CCOP applicant and corresponding research base(s) at the time of application submission. This agreement must specifically state how the problem of competing protocols is to be resolved. Initial affiliations must be maintained during the first three-year funding cycle. Unusual circumstances may require changes in research base affiliations, subject to NCI staff approval. CCOP affiliations with centers and regional cooperative groups must be geographically appropriate. A CCOP applicant may not bypass regional research base programs to establish ties with distant centers unless there is clear justification and NCI staff approval.

F. The conditions of affiliation with a maximum of two multi-disease research bases (with two, only one may be a cooperative group) and three special category research bases must be provided in the CCOP Research Base Affiliation Agreement(s).

G. Quality-controlled clinical research data is a performance requirement. Assurance of quality is the joint responsibility of the CCOP and its research base affiliate(s). Quality control procedures, operational in the center or group, will be applied to the CCOPs and must be specified in the CCOP-Research Base Affiliation Agreement.

H. Each CCOP must have a defined space for administrative activities and administrative personnel which will serve as a focus for data management, quality control, and communication.

I. Allocation of CCOP funds to support community and research base costs for receipt, handling, and analysis of patient data should be specified in the written agreement between the CCOP applicant and its research base. Allowable items in the budget would be for administrative personnel, data handlers, and study assistants, supplies and services directly related to study activities (e.g., processing and sending material for pathology review, processing and sending port films for radiation therapy quality control) and limited travel to meetings directly related to study activities. Physician compensation would be allowable only for time spent on the project other than clinical care. Total funding as well as allowable physician compensation may be increased proportionately for participating in future NCI initiated cancer control activities. Initial funding is to be for three years.

J. The following administrative requirements prior to award will apply to all CCOP programs.

1. Management of Federal Funds

This ability includes the following basic requirements:

- A formal organizational structure capable of managing the project and safeguarding the disposition of federal funds;
- Adequate cost accounting and bookkeeping procedures including the capacity to separately monitor federal funds;
- Time and effort policies to account for personnel costs; and
- Accountability for all equipment, supplies and other necessary project expenditures.

2. Mandated Assurances

These may be found in the Grant Application Form 398 (Rev. 5/80):

- Civil Rights (page 4)
- Handicapped Individuals (page 4)
- Sex Discrimination (page 4)
- Protection of Human Subjects (pages 3 and 14)

3. Cost Sharing

The Appropriation Act for the DHHS requires that grantee institutions share in the cost of activities supported by research grants. Some direct or indirect contribution should be made to the project.

4. Indirect Costs

Unless directed otherwise, succesful applicants who have not negotiated an indirect cost rate must do so. The negotiation of the indirect cost rate may begin just prior to, or immediately following, notification of grant award. Guidance on this requirement will be made available by the NCI upon approval of the application.

5. Payment Procedures

Payments for grants awarded by the NIH are made through the Departmental Federal Assistance Financing System (DFAFS). Guidance for payment will be made by the NCI to successful applicants at the time of award. Under no circumstances will pre-award costs, (i.e., expenses incurred prior to actual funding) be allowed.

K. The following operational prerequisites are expected:

1. A list of protocols which will be used by the CCOP to meet patient accrual requirements must be stated in the initial application. Protocols initiated after the initial award must be filed with DRCCA staff. Protocol review and approval procedures for the CCOP will be consistent with that of the research base.

2. Each CCOP agrees to maintain a new patient log or minimal registry to include age, sex, primary site of cancer, stage of disease, and treatment disposition for the potentially eliible patient pool.

3. Radiotherapy equipment must have its calibration verified by the Radiological Physics Center (RPC) or one of the regional Centers for Radiological Physics (CRP) in order for institutions to participate in this program. Information is available upon request. Prior to award, a letter of compliance will be provided.

4. Each CCOP agrees to accept periodic on-site monitoring by representatives of its research base(s) or NCI or an NCI designee. The purpose of such on-site monitoring may include monitoring of use of investigational drugs, accuracy of data recording, completeness of reporting adverse drug reactions, protocol accrual and quality control analysis, fiscal and administrative review.

5. Each CCOP agrees to an annual review of its progress by the executive committee of its research base(s) and DRCCA staff. This review will include, but not be limited to, overall case accrual, accrual to high priority protocols, patient eligibility, patient evaluability, and timeliness and quality of data reporting. This annual review may be the basis for probationary status or adjustment in funding.

V. CCOP AND RESEARCH BASE(S)--COOPERATIVE ACTIVITIES

In preparation for submission of the application, negotiations between the CCOP and the research base should result in agreement about protocol participation, method of support for the research base (for data management) and the expected cost to the research base as a result of case accrual. Cooperation is anticipated in:

A. Planning for program development and training of support personnel (e.g., data managers, study assistants, oncology nurses, etc.).

B. Developing and/or making available appropriate clinical research protocols.

C. Establishing standards for surgery and pathology reporting procedures of the research base, community members and affiliates.

D. Holding regular meetings of the research base, community members and affiliates for review of ongoing research activities, planning of future activities, and relate professional education.

E. Instituting quality control procedures for data recording, protocol compliance, and reporting of adverse reactions.

F. Instituting control procedures for treatment planning such as standardization of radiation equipment, doses and fields.

G. Establishing an organizational mechanism for the relationship between the CCOP and research base(s) and the reimbursement of research base costs. Circumstances may vary from CCOP to CCOP.

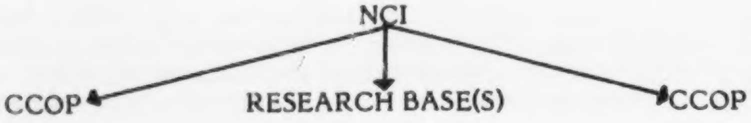
VI. RESEARCH BASE PARTICIPATION

The general function of a research base is to collaborate to a degree appropriate to the applicant CCOP, providing protocol access, assistance in data quality control and feedback information on clinical trial performance. The CCOP-Research Base Agreement should define mechanism for community participants to have input as active research base members.

Each research base will need to develop a plan to support additional administrative and data management functions and to provide annual reports on protocol accrual and quality control analysis for review by DRCCA staff.

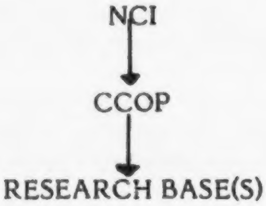
Three options for research support are available. The research base(s) participating with approved CCOPs may receive appropriate support through a supplement to their existing primary grant which will be subject to appropriate review and approval processes. Costs will be based on anticipated protocol participation and data management expectations, negotiated by NCI staff after appropriate review. (See Example 1)

Example 1.


NCI
CCOP
RESEARCH BASE(S)
CCOP

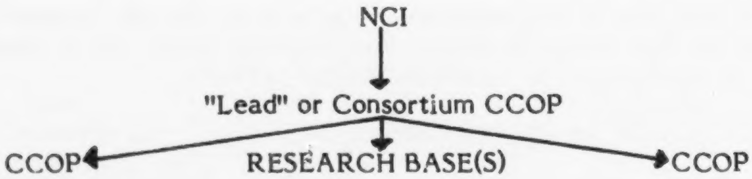
An alternative method of fiscal support for the research bases may come through a single CCOP (See Example 2);

Example 2.


NCI
CCOP
RESEARCH BASE(S)

or a lead CCOP (See Example 3);

Example 3.


NCI
"Lead" or Consortium CCOP
CCOP
RESEARCH BASE(S)
CCOP

Research Base Options

A. A Multi-disease Research Base

(may choose one or two)

1. NCI-funded comprehensive and clinical cancer centers

2. Cooperative Groups

   a. Cancer and Leukemia Group B (CALGB)
   b. Eastern Cooperative Oncology Group (ECOG)
   c. North Central Cancer Treatment Group (NCCTG)
   d. Northern California Oncology Group (NCOG)
   e. Southeastern Cancer Study Group (SEG)
   f. Southwest Oncology Group (SWOG)
   g. Mid-Atlantic Oncology Group-Georgetown University
   h. Piedmont Oncology Group

B. Special Category Research Bases (maximum three)

1. Pediatric Oncology Research Base (may choose one)

    a. Childrens Cancer Study Group (CCSG)
    b. Pediatric Oncology Group (POG)

2. Other Research Bases (may choose more than one)

    a. Gynecologic Oncology Group (GOG)

    b. Radiation Therapy Oncology Group (RTOG) - Must clarify patient allocation if protocols overlap with category A choices.

    c. National Surgical Adjuvant Breast and Bowel Project (NSABP) - participation in surgical protocols (B-06 is an example) falls in this category. Participation in the adjuvant protocols of this group may be a potential conflict with the protocols of a category A research base and allocation of patients must be clarified and both NSABP and the category A research base must concur in this allocation plan.

    d. Gastro-Intestinal Tumor Study Group (GITSG) - participation in the protocols of this group may conflict with protocol of a category A research base and allocation of patients must be clarified and both GITSG and the category A research base must concur in this allocation plan.

    e. Lung Cancer Study Group (LCSG) - participation in the protocols of this group may conflict with protocols of a category A research base and allocation of patients must be clarified and both LCSG and the category A research base must concur in this allocation plan.

VII. MECHANISM OF SUPPORT

The CCOP awards will be made as Cooperative Agreements. These are assistance relationships supporting projects that require substantial collaboration and involvement with NCI staff. Depending on individual CCOP costs, up to 200 awards with a total not to exceed 10 million dollars per year, will be allocated for this program. NCI anticipates making multiple awards under this request. Awards will be for periods of three years to establish the initial capabilities of the participants. Repetitive RFAs are planned. Renewal of grants after three years will be contingent upon satisfactory review of a competing application by a scientific peer review committee and the National Cancer Advisory Board.

VIII. LETTER OF INTENT

Letters of intent should precede the submission of the grant application and are due August 23, 1982. These are to be detailed documents suitable for review for responsiveness to this Request for Applications. Those judged to be non-responsive will be returned with an explanation and the applicants will be encouraged to respond to future issuances of the RFA for Community Clinical Oncology Programs.

The letter of intent should address the following issues succinctly (about one page per topic):

A. A description of the CCOP organization (including catchment area and patient availability).

B. Existing cancer control activities in the area of the CCOP.

C. Names and type of practice (e.g., medical oncology, internal medicine) of participants.

D. Research affiliations, planned protocol participation and estimated patient accrual per protocol.

The total pages for the letter should not exceed 15 pages. Applicants whose letter of intent is responsive will be notified and asked to submit full applications.

IX. METHOD OF APPLYING

Complete applications are due on or before close-of-business November 9, 1982. Applications must addres all requirements as presented in this RFA. Applications for CCOPs and Research Bases should be submitted on Form PHS 398, (revised 5/80), the application form for the traditional research project grant, which is available in the business or grants and contracts office at most academic institutions and research institutions, or from the Division of Research Grants, NIH, Bethesda, Maryland 20205. This CCOP application request has no page limitation; however, applications should be as concise as possible. The words "Community Clinical Oncology Program" should be typed in bold letters on line number 2 of the face page of the application and also on the outside of the mailing package.

Additionally, a brief covering letter should accompany the application indicating that it is being submitted in response to this request. The original and 6 copies of the application should be submitted to the Division of Research Grants, NIH, as directed in the Grant Application Instructions. Two additional copies should be sent to:

Referral Officer, Grants Review Branch
Division of Extramural Affairs
National Cancer Institute
Westwood Building - Room 826
5333 Westbard Avenue
Bethesda, Maryland 20205

X. REVIEW PROCEDURES AND CRITERIA

A. Review Method

Applications responsive to this RFA will be reviewed by an appropriate peer review panel of the National Institutes of Health. Final review is provided by the National Cancer Advisory Board.

B. Availability of Patients

Reviewers will assess the ability of the CCOP to meet the requirement for entering a minimum of 50 evaluable patients per year on clinical trials. Evaluable patients are those eligible individuals who have had the appropriate diagnostic work-up, treatment, and follow-up to complete the study as outlined in the protocol. Available patients are those seen by CCOP physicians who may be considered eligible for study. Only the patients available to the CCOP applicants will be counted toward the denominator constituting the 10% minimum requirement. The population referral area should be specified. Information (tumor registry and/or clinic visit data) should be provided which demonstrate the number of cases (by disease category) seen per year by the participating physicians and/or institutions during 1980 and 1981. An explanation of how the numbers were derived should be provided. Special attention should be given to those disease categories for which the CCOP has agreed to enter patients on protocol.

C. Physicians

Reviewers will consider the availability, training, experience and commitment of participating physicians as appropriate for the treatment of patients on the protocols in which the CCOP has agreed to participate (e.g., if protocols require radiotherapy, the availability and qualifications of radiation therapists will be considered, etc.). The work experience of participant oncologists gained from residency, fellowship, or post training in the entry and treatment of cancer patients on research trials should be described. A curriculum vitae (not to exceed two pages each) and a signed statement of commitment to enter patients on selected protocols chosen by the CCOP from each participating physician should be provided.

D. Facilities and Equipment

Reviewers will appraise the availability of treatment facilities, both inpatient and outpatient; these should be described in the application. If the CCOP plans to enter patients on studies involving radiation therapy, available equipment should be described. A statement of commitment from each participating institution should be provided.

E. Other Existing Cancer Control Activities

Reviewers will consider the quality and effectiveness of existing cancer control efforts. These include education programs, tumor board conferences, patient management guideline development, formal supportive care efforts, and participation in formal cancer control network, outreach and research programs. Such activities will be regarded as a positive feature in an application and an indication of the institutional commitment to quality cancer care. No one activity will be considered a requirement.

F. Affiliation Agreements

Reviewers will appraise the affiliation agreements with research bases provided in the application. The appropriateness of the affiliation and of the protocols chosen, the adequacy of quality assurance mechanism for both treatment and data, and the adequacy of investigational drug monitoring procedures and data management procedures will be considered.

G. Principal Investigator

Reviewers will consider the qualifications and experience of the principal investigator related to his/her ability to organize and manage a community oncology program.

H. Support Personnel

The qualifications and experience of all proposed non-physician personnel will be assessed by the reviewers. A clear description of the proposed duties for each named and to-be-named position should be provided.

XI. NATURE OF COOPERATION WITH NCI STAFF: TERMS OF AWARD

A. Protocol Review

Protocol review and approval procedures for the CCOP will be consistent with that of the research base.

B. Quality Control

The DRCCA staff will periodically review mechanisms developed to apply clinical trials quality control procedures in the community setting.

C. Data Management

DRCCA staff will have access to all data and will periodically review data management by the group. Data must be available for external monitoring if required by NCI.

D. Investigational Drug Management

DCT staff will advise investigators of specific requirements and changes in requirements concerning investigational drug management that the Food and Drug Administration (FDA) may mandate. Investigators performing trials under Cooperative agreements will be expected, in cooperation with the NCI, to comply with all FDA monitoring and reporting requirements for investigational agents.

E. Program Review and Performance Reporting Requirements

Annual progress reports will be submitted to the DRCCA, NCI. Report format will be provided by the DRCCA staff to the CCOPs. Following the receipt of these reports, the CCOP's progress will be reviewed by the DRCCA staff in collaboration with the affiliated research bases. Reviews will be based on performance criteria presented in this RFA and as outlined in CCOP-Research Base Agreements.

XII. SOURCES OF FURTHER INFORMATION

Inquiries related to (1) the identification of eligible research base options and (2) general information on CCOPs should be directed to:

Office of Cancer Communications
Public Inquiries Section
Building 31 - Room 10A18
9000 Rockville Pike
Bethesda, Maryland 20205

Residents of all states but Maryland may call the toll free number:

(800) 638-6694
(800) 638-6070 Alaska and Hawaii

Maryland residents may call:

(800) 492-6600

Correspondence related directly to application development and letters of intent should be directed to:

Robert W. Frelick, M.D.
Program Director
Division of Resources, Centers and
Community Activities
National Cancer Institute
Blair Building - Room 7A01
8300 Colesville Road
Silver Spring, Maryland 20910

Telephone: (301) 427-8708

Questions pertaining to business matters should be directed to:

John G. Dell
Grants Management Specialist
Grants Administration Branch, OD
National Cancer Institute
Westwood Building - Room 854
5333 Westbard Avenue
Bethesda, Maryland 20205

Telephone: (301) 496-7444

V. CCOP AND RESEARCH BASE(S)--COOPERATIVE ACTIVITIES

In preparation for submission of the application, negotiations between the CCOP and the research base should result in agreement about protocol participation, method of support for the research base (for data management) and the expected cost to the research base as a result of case accrual. Cooperation is anticipated in:

A. Planning for program development and training of support personnel (e.g., data managers, study assistants, oncology nurses, etc.).

B. Developing an/or making available appropriate clinical research protocols.

C. Establishing standards for surgery and pathology reporting procedures of the research base, community members and affiliates.

D. Holding regular meetings of the research base, community members and affiliates for review of ongoing research activities, planning of future activities, and relate professional education.

E. Instituting quality control procedures for data recording, protocol compliance, and reporting of adverse reactions.

F. Instituting control procedures for treatment planning such as standardization of radiation equipment, doses and fields.

G. Establishing an organizational mechanism for the relationship between the CCOP and research base(s) and the reimbursement of research base costs. Circumstances may vary from CCOP to CCOP.

VI. RESEARCH BASE PARTICIPATION

The general function of a research base is to collaborate to a degree appropriate to the applicant CCOP, providing protocol access, assistance in data quality control and feedback information on clinical trial performance. The CCOP-Research Base Agreement should define mechanism for community participants to have input as active research base members.

Each research base will need to develop a plan to support additional administrative and data management functions and to provide annual reports on protocol accrual and quality control analysis for review by DRCCA staff.

Three options for research support are available. The research base(s) participating with approved CCOPs may receive appropriate support through an administrative supplement to their existing primary grant which will be subject to the usual approval process. Costs will be based on anticipated protocol participation and data management expectations, negotiated by NCI staff with appropriate consultation.

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11/9

NIH GUIDE for GRANTS and CONTRACTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Vol. 11, No. 9, August 13, 1982

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HAVE YOU MOVED?

If your present address differs from that shown on the address label, please send your new address to: Grants and Contract Guide Distribution Center, National Institutes of Health, Room B3BN10, Building 31, Bethesda, Maryland 20205, and attach your address label to your letter. Prompt notice of your change of address will prevent your name from being removed from our mailing list.

The GUIDE *is published at irregular intervals to announce scientific initiatives and to provide policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in grants and contracts activities administered by the National Institutes of Health.*

Two types of supplements are published by the respective awarding units. Those printed on yellow paper concern contracts: solicitations of sources and announcement of availability of requests for proposals. Those printed on blue paper concern invitations for grant applications in well-defined scientific areas to accomplish specific program purposes.

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Vol. 11, No. 9, August 13, 1982

NOTICE

DEADLINE FOR SUBMISSION OF ASSURANCES OF COMPLIANCE WITH REVISED HUMAN SUBJECTS PROTECTION REGULATIONS

On January 26, 1981, the Department of Health and Human Services (DHHS) published final regulations amending basic DHHS policy for the protection of human research subjects. Institutions holding an Assurance of Compliance were encouraged to implement new provisions of the regulations prior to the negotiation of a revised Assurance of Compliance. Since August, 1981, the Office for Protection from Research Risks (OPRR) has been negotiating Assurances of Compliance with the new regulations.

This notification establishes a deadline of December 31, 1982, for submission of a general (Multiple Project) assurance prepared in accord with DHHS regulations published in the Federal Register on January 16, 1981 (46 FR 8366).

Institutions are encouraged to submit an Assurance of Compliance at the earliest possible date. A sample assurance is available from OPRR (301 - 496-7041). Although it is possible that approval of a multiple project assurance might not be transmitted until sometime after December 31, 1982, institutions may continue to function under their former assurance until such time as approval for the revised assurance is given. Special (Single Project) assurances will continue to be approved on a single project basis. GENERAL ASSURANCES WHICH HAVE NOT BEEN REVISED TO MEET THE 1981 REQUIREMENTS AND SUBMITTED TO OPRR WILL BE TERMINATED EFFECTIVE JANUARY 1, 1983.

NOTICE

SPECIAL CONSIDERATION FOR HEALTH PROFESSIONAL STUDENTS SEEKING RESEARCH CAREERS

NIH training Program Directors are reminded that NIH training grants may support individuals who wish to interrupt their medical, veterinary, dental, or other professional school studies for a year or more to engage in full-time research training before completing their professional degrees. The stipend should be paid at the predoctoral level of $5,040 per year. Program Directors are advised to consult with NIH staff in the awarding Institute before appointing such trainees unless such training was part of the approved training grant. National Research Service Award (NRSA) stipends may not support studies leading to the M.D., D.O., D.D.S., D.V.M., or other similar medical degrees, nor may they be used to support residencies.)

REQUEST FOR COOPERATIVE AGREEMENTS APPLICATIONS: RFA

NIH-NCI-DCT-CTRP-82-13

STUDIES OF ACQUIRED IMMUNO-DEFICIENCY SYNDROME (KAPOSI'S SARCOMA AND OPPORTUNISTIC INFECTIONS)

NATIONAL CANCER INSTITUTE

Application Receipt Date: October 22, 1982

I. BACKGROUND INFORMATION

The National Cancer Institute (NCI) invites applications for Cooperative Agreements to support "Working Group" research projects into the etiology and treatment of patients with Kaposi's sarcoma (KS), unexplained opportunistic infections (OI) or other manifestations of acquired immunodeficiency. Since June, 1981, the Centers for Disease Control in Atlanta have learned of an increased occurrence of KS, Pneumocystis carinii pneumonia, and other serious OI's concentrated among homosexual men in the United States. Investigation to date has identified an apparently new syndrome which has reached epidemic proportions. In addition to the association with homosexuality there is an underlying state of profound immunosuppression characterized by marked suppression of peripheral blood inducer/helper T-lymphocytes. Affected patients have very often presented with a symptom complex of chronic fever, weight loss and lymphadenopathy as a prodrome to the development of KS or serious OI. To date epidemiologic studies have failed to reveal an etiology, although abuse of certain drugs (especially nitrites) and previous or concomitant infection with certain viruses and other agents have been common.

This serious public health problem deserves intensive investigation. In addition, research into this epidemic could yield important new information on the etiology of cancer in man. The purpose of this RFA is to encourage such research by providing support to institutions possessing an interest in the problem, as well as a population of affected patients and/or laboratory facilities and personnel appropriate to the conduct of such research.

It is intended that this research will be conducted in the context of a "Working Group," i.e., a group of institutions carrying out various research projects funded as a result of this RFA or other mechanisms. NCI staff will serve as a resource of information and will work to facilitate exchange of information and material

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This program is described in the Catalog of Federal Domestic Assistance No. 13.395, Cancer Treatment Research. Awards will be made under the authority of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended; 42 USC 282) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

between involved investigators. It is NCI's assessment that such collaboration between investigators will permit achievement of the goals of this RFA - i.e., definition of etiology, treatment and prevention - in the most rapid and efficient manner possible.

II. RESEARCH GOALS AND SCOPE

Studies to be proposed should stress innovative approaches to this problem and should include any or all of the following three components:

1) Epidemiologic studies designed to identify risk factors in patients with KS, the acquired immunodeficiency syndrome or prodromal conditions, along with appropriate control populations.

2) Laboratory research projects in etiology and pathophysiology. These would inclue both in vitro and in vivo studies in such areas as immunology, microbiology, virology, and toxicology, and would comprise studies of the immunodeficiency syndrome, prodromes, Kaposi's sarcoma and opportunistic infections.

3) Innovative treatment and prevention research projects involving patients with Kaposi's sarcoma, unexplained opportunistic infections, other manifestations of acquired immunodeficiency, or prodromes to this syndrome. Most appropriate would be therapy studies linked to etiologic hypotheses or observations.

Encouraged, but not required, are applications from institutions or consortia possessing resources and expertise in all areas. All applicants should clearly document access to an adequate patient population base (either directly or through explicit collaboration) since a major criterion for review will be an ability to complete meaningful studies in a reasonable period of time.

The NCI plans semi-annual meetings of the Working Group. It is hoped that these meetings will provide an opportunity for the development of collaborative arrangements between investigators performing complementary research. At this time it is impossible to explicitly outline the nature of such arrangements since the scope of projects to be funded is unknown. An example, however, would be the provision of biological specimens from patients enrolled in epidemiologic studies to investigators performing in vitro studies of immune function. It is NCI's assessment that this cooperation will hasten the resolution of the important questions relevant to this epidemic and will result in a more efficient allocation of funds. It is anticipated that NCI staff will play a key role in coordinating and facilitating such collaboration as various research activities evolve. Further details of this involvement are outlined below under "Terms of Award."

III. MECHANISM OF SUPPORT

Awards will be made as Coopperative Agreements. These are assistance relationships involving substantial involvement with NCI staff, as outlined under Part IV, "Terms of Award." NCI anticipates making multiple awards as a result of this request. It is anticipated that a total of $1,000,000 will be set aside to fund the initial year's awards. Awards will be made for project periods of three to five years. Future renewal applications will not compete for earmarked funds. All policies and requirements which govern the grant programs of the PHS apply, including the requirement for cost sharing.

IV. NATURE OF COLLABORATION WITH NCI STAFF: TERMS OF AWARD

This section outlines the collaboration between recipients of these cooperative agreements and NCI program staff.

A. Scientific Resources

1. The Awardees shall develop research protocols and plans in accord with their individual interests and strengths as well as the minimum requirements included in these terms of award.

2. The NCI staff will serve as a resource of information on the activities of various members of the working group and will act to facilitate collaboration among involved researchers. It is in the context of the Working Group semi-annual meetings that the awardees, with the assistance of NCI staff, will identify and develop these collaborative areas.

B. Treatment Studies

NCI approval will be required for all treatment protocols developed following award. NCI staff will hold regular protocol review meetings chaired by the Associate Director, Cancer Therapy Evaluation Program, NCI, or his designee. The primary purposes of this review are 1) to assure that the proposed research is in compliance with all FDA requirements for NCI-funded clinical treatment research and 2) to identify and prevent undesirable duplication of efforts. Protocols may be disapproved by NCI on the basis of patient safety and toxicity, obvious duplication, or failure to meet FDA regulations, particularly those concerning NCI-sponsored investigational drugs.

If a proposed protocol is found to be unacceptable for any of the above reasons, the specific reasons for lack of approval will be communicated to the investigator within 30 days of protocol receipt by the NCI. NCI staff will work with the investigators to develop a mutually acceptable protocol compatible with the research interests and needs of the working group and the NCI.

NCI will establish an appeals process for determining the suitability of treatment protocols it has found unacceptable on initial review, and for which a mutually acceptable protocol cannot be arrived at through discussions between the group and NCI staff. An arbitration panel composed of one working group participant, one NCI nominee, and a third member with clinical trials expertise chosen by the other two members will be formed to review NCI decisions. This NCI arbitration process in no way affects the right of a recipient to subsequently appeal an adverse determination using the NIH informal appeals system and the formal Department of Health and Human Services procedures. If the investigator proceeds with performance of a protocol disapproved by the arbitration panel, the results of that study will be subject to careful monitoring and targeted for peer review when the competitive renewal application is under consideration. In addition, the NCI may withdraw the portion of funding designated for a disapproved protocol, if the grounds for disapproval are patient safety and toxicity, or unnecessary duplication.

V. REVIEW PROCEDURES AND CRITERIA

A. Review Method

All applications submitted in response to this RFA will be reviewed in competition with each other by:

1. an NIH peer review group and
2. the National Cancer Advisory Board

B. Review Criteria

Applications must be responsive to this RFA, in the sense of being directed towards the attainment of the stated programmatic goals (see II. GOALS AND SCOPE). If the application is judged by the National Institutes of Health to be unresponsive, the applicant will have the opportunity of having the application considered along with other unsolicited applications received by the National Institutes of Health.

The factors considered in evaluating each response to this RFA will be:

1. Scientific merit of research approach, design, and methodology.
2. Research experience and competence of the Principal Investigator and staff to conduct the proposed studies.
3. Adequacy of time (effort) which the Principal Investigator and staff would devote to the proposed studies.
4. Adequacy of existing/proposed facilities and resources. This includes adequacy of patient resources to ensure completion of meaningful studies in a reasonable period of time.
5. Scientific, technical or medical significance and originality of proposed research.
6. Reasonableness of proposed costs.

VI. METHOD OF APPLYING

A. Format of Applications

Applications must be submitted on form PHS 398 (Rev. 5/80), the application form for research grants. Application kits are available at most institutional business offices, or may be obtained from the Division of Research Grants, NIH. The format and detail applicable to regular research grant applications should be followed, and the requirements specified under Review Criteria (V.B.) must be fulfilled. The NCI plans semi-annual meetings of the Working Group. Applicants are encouraged to include in their budgets travel funds for one investigator to two meetings per year in Bethesda, Maryland. The words "PROPOSAL IN RESPONSE TO RFA NIH-NCI-DCT-CTEP-82-13" should be typed across the top of the face page of the application. Additionally, a brief covering letter should accompany the application indicating that it is being submitted in response to this request. The original and six copies of the application should be submitted to the Division of Research Grants, NIH, as directed in the Grant Application Instructions. An additional two copies should be sent to the following:

Dr. Harold Waters
Chief, Special Review Branch
Division of Research Grants
Westwood Building - Room 2A16
Bethesda, Maryland 20205

All curricula vitae should be limited to three pages each.

This is a one-time request for applications. NCI has no plans to reissue this announcement at any future date. The single deadline for receipt of applications is October 22, 1982. Applications received after this date will be considered unresponsive and will be returned without additional review.

Investigators interested in submitting applications in response to this announcement are encouraged to contact:

John Y. Killen, Jr., M.D.
Head, Medicine Section
Clinical Investigations Branch
Cancer Therapy Evaluation Program
Landow Building - Room 4A14
7910 Woodmont Avenue
Bethesda, Maryland 20205

Telephone: (301) 496-2522

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

NIH-NCI-DCCP-SPB-82-1

EPIDEMIOLOGIC STUDIES OF RARE TUMORS

NATIONAL CANCER INSTITUTE

Application Receipt Date: November 1, 1982

The Division of Cancer Cause and Prevention (DCCP) of the National Cancer Institute (NCI) invites grant applications from interested investigators for epidemiologic studies of rare tumors. Epidemiologic investigations have tended to emphasize the more prevalent forms of cancer. A number of tumors which occur with less frequency have lacked the research interest of investigators.

Grants are awarded to nonprofit and profit organizations and institutions, governments and their agencies, and occasionally to individuals. This type of grant solicitation (the RFA) is utilized when it is desired to encourage investigator-initiated research projects in areas of special importance to the National Cancer Program. Applicants funded under the RFA are supported through the customary NIH grant-in-aid, in accordance with PHS policies applicable to Research Project Grants, including cost-sharing. The RFA solicitation, however, represents a single competition, with a specified deadline for receipt of applications. All applications received in response to the RFA are usually reviewed by the same National Institutes of Health (NIH) Initial Review Group (IRG). The specific deadline for the receipt of response to this RFA is November 1, 1982. Applications should be prepared and submitted in accordance with the aims and requirements of the following sections:

I Background Information
II Objectives and Scope
III Mechanisms of Support
IV Review Procedures and Criteria
V Method of Applying
VI Inquiries

I. BACKGROUND INFORMATION

Forty-two percent of all malignant cancers are accounted for by cancer of the three primary sites of colon/rectum, breast and lung. Although males generally experience higher cancer incidence rate than females, striking differences occur among race, sex groups, and geographic areas with respect to the incidence of cancer of various sites.

This program is described in the Catalog of Federal Domestic Assistance No. 13.393, Cancer Cause and Prevention Research. Awards are under authorization of the Public Health Service Act, Section 301(c) and Section 402 (Public Law 78-410, as amended, 42 USC 241, 42 USC 282) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

Among the less frequently studied tumors from which important informtion may be gained are, for example, malignancies of the thyroid (1.3% of all malignant tumors); anus, anal canal and anorectum (0.2%); soft tissues, including heart (0.6%); bone and joints (0.2%) male breast (0.1%); penis (0.1%) and salivary gland tumors (0.3%).*

The study of rare tumors may provide insight and establish causal associations with environmental risk factors, as for example, DES and clear cell adenocarcinoma in offspring; and vinyl chloride and angiosarcoma of the liver. Investigations of rare tumors may also lead to better understanding of more common tumors, for example, male breast cancer and female breast cancer. In addition, studies which compare risk factors in low and high incidence areas may provide clues for further environmental and/or familial studies of possible etiology.

II. OBJECTIVES AND SCOPE

The primary objective of this RFA is to encourage studies aimed at the elucidation of causal factors in the development of rare cancers. The tumors to be investigated will not be specified by this RFA. Potential etiologic factors to be addressed could include, for example, occupational/environmental exposures, genetic/familial factors, diet, drug use (therapeutic and other), cigarette smoking, behavioral factors, or any other variables which the investigator chooses to examine.

This RFA proposes to fund research to generate causative/etiologic hypotheses, to provide clues of association; and/or to develop improved research design/methodology for the study of rare cancers. Such studies can provide the basis for more extended research designed to provide information on etiology and the natural history of specific rare malignant tumors or to develop studies which may provide insight into the more common tumors. These applications may include studies to determine the feasibility of studying specific rare cancers.

It is anticipated that subsequent case-control or cohort studies of less common tumors developed from these initial studies could compete in the traditional investigator-initiated research grant program (R01).

III. MECHANISM OF SUPPORT

This RFA will use the traditional National Institutes of Health grant-in-aid. The RFA identifies the scope of the Institute's interest. It is expected that responsibility for the planning, direction and execution of the proposed research will be solely that of the applicant. The intent is to fund a maximum of eight (8) projects, with total costs amounting to approximately $400,000 for the first year. This funding level is dependent on the receipt of a sufficient number of applications of high scientific merit.

This award may not be used to supplement support for an ongoing project.

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* Percent distribution of all malignant cases in Surveillance, Epidemiology and End Results: Incidence and Mortality Data 1973-77, NCI Monograph No. 57, June 1981. NIH Publication No. 81-2330.

IV. REVIEW PROCEDURES AND CRITERIA

Applications must be responsive to this RFA, in the sense of being directed towards the attainment of the stated programmatic goals and fall within one or more of the specified research categories (see II. OBJECTIVES AND SCOPE). If the application is judged by the National Cancer Institute not to be responsive, the applicant may have it considered as a traditional R01, along with other applications in the next regular review cycle. Arrangements will be made by the Division of Research Grants for the review of responsive proposals.

The factors considered in evaluating each response to this RFA will be:

1. Scientific merit of research approach, design, and methodology.
2. Research experience and competence of the Principal Investigator and staff to conduct the proposed studies.
3. Adequacy of time (effort) which the Principal Investigator and staff would devote to the proposed studies.
4. Adequacy of existing/proposed facilities and resources. Applications which specify a proposed use of human specimens need to provide assurance and details concerning the nature, source, and availability of those specimens.

V. METHOD OF APPLYING

A. Format of Application

Applications must be submitted on form PHS 398 (revised 5/80), the application form for research project grants. Application kits are available at most institution business offices, or may be obtained from the Division of Research Grants, NIH. The conventional presentation in form and detail applicable to regular research grant applications should be followed, and the requirements specified under Review Criteria (Section IV above) must be fulfilled.

The words "RESPONSE TO RFA NIH-NCI-DCCP-SPB-82-1, EPIDEMIOLOGIC STUDIES OF RARE TUMORS" must be typed in bold letters across the face page of the application.

B. Application Procedure

The completed original application and six (6) copies should be sent or delivered to:

Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205

To ensure their review, applications should be received by November 1, 1982. If applications are received after that date, the applicant will have the opportunity of having them considered, along with other unsolicited applications, in the next regular review cycle. Also, the Division of Research Grants (DRG) will not accept any application in response to this announcement, which is the same as one currently being considered by any other NIH awarding unit. A copy of the application should also be sent to Dr. Millner at the address shown below.

VI. INQUIRIES

Inquiries may be directed to:

Elaine S. Millner, Dr. P.H.
Special Programs Branch
Division of Cancer Cause and Prevention
National Cancer Institute
Landow Building - Room 8C16
Bethesda, Maryland 20205

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

NIH-NCI-DCCP-SPB-82-11

BIOCHEMICAL EPIDEMIOLOGY

NATIONAL CANCER INSTITUTE

Application Receipt Date: November 15, 1982

I. BACKGROUND

Although a significant proportion of human cancers are thought to be attributable to life style and other environmental factors and therefore potentially preventable, the task of identifying the effects of specific factors and evaluating their relative importance is an enormous one. The process of induction and progression of human cancer is exceedingly complex, multiple exposure to a variety of agents over time is the rule rather than the exception, past exposure is difficult to assess, host factors which may influence susceptibility are poorly understood, and the importance of promoting and/or anticarcinogenic exposures in humans have not been adequately defined.

Epidemiologic studies have resulted in the identification of factors which appear to increase or decrease cancer risk and have suggested the importance of host-susceptibility factors. The usual epidemiologic techniques, however, have been limited in their ability to reach firm conclusions by the difficulties in defining past carcinogen exposure levels and susceptibility states, in measuring low levels of risk, in evaluating directly host environmental interactions, and in identifying dietary determinants of cancer. Fortunately, a variety of sensitive and specific laboratory methods are now becoming available which are likely to facilitate epidemiologic investigations by providing better measures of exposure to initiators, promoters, anticarcinogens and inhibitors of carcinogenesis. Increased collaboration between laboratory scientists and epidemiologists in the application of these emerging techniques would be highly desirable.

Modifying factors related to diet and nutrition have been implicated in several epithelial cancers including those of the gastrointestinal tract and reproductive organs. Hence these types of cancer (among others) might be especially suitable for collaborative studies involving epidemologists and experimentalists, including biochemists, analytical chemists, immunologists, and nutritionists.

This program is described in the Catalog of Federal Domestic Assistance No. 13.393, Cancer Cause and Prevention Research. Awards are under authorization of the Public Health Service Act, Section 301(c) and Section 402 (Public Law 78-410, as amended; 42 USC 241; 42 USC 282) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

II. GOALS AND SCOPE

The purpose of this RFA is to stimulate epidemiologic/laboratory collaboration in developing and/or applying objective measures useful in studying the etiology of human cancer. Respondents must demonstrate expertise in both sound epidemiologic design and laboratory methods. Appropriate interaction between epidemiologic and laboratory expertise should be evident in all phases of the proposed research from planning through implementation, analysis, and reporting. Examples of types of laboratory measurements which might be appropriate would include: 1) assessment of specific host factors which might influence susceptibility to carcinogenesis (e.g., DNA repair assays, examination of chromosomal defects or susceptibility to cell transformation, assays for immunocompetence or analysis of serum levels of vitamins or micronutrients), 2) detection and quantitation of chemical carcinogens or their metabolites in tissues or body fluids (e.g., analytical chemical measurements, mutagenesis assays or immunologic detection techniques), 3) measurement of interaction of specific agents with cellular target molecules (e.g., adduct formation with proteins and nucleic acids, excretion levels of excised adducts or markers of altered gene expression). Applications should be consistent with the state-of-the-art; feasibility studies or pilot studies are acceptable when developmental research is needed as preparation for a population study.

III. MECHANISM OF SUPPORT

This RFA will use the traditional National Institutes of Health research project grant. Responsibility for the planning, direction and execution of the proposed research will be solely that of the applicant. The total project period for applications submitted in response to the present RFA should not exceed three years. The intent is to fund several individual research project grants, with total costs amounting to approximately $1.5 million for the first year. This funding level is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of the National Cancer Institute, the award of grants pursuant to this RFA is also contingent upon the availability of funds for this purpose. Renewal applications will compete with all other unsolicited applications received by the NCI. NIH policies governing regular research project grants will apply to applications received in response to this request.

IV. REVIEW PROCEDURES AND CRITERIA

A. Review Procedure

Upon receipt in the Division of Research Grants, applications will be reviewed for responsiveness. If an application is judged to be nonresponsive, the applicant will be contacted and given an opportunity to have it considered along with other unsolicited grants received by NIH for this cycle.

Proposals responsive to this solicitation will be reviewed in competition with each other on a nationwide basis. The initial review will be for scientific merit and will be carried out by an appropriate peer review group. The secondary review for relevance and responsiveness to the announcement will be made by the National Cancer Advisory Board.

B. Review Criteria

Applications should be responsive to the RFA and, therefore, relevant to the program goals of the National Cancer Institute. Those fctors considered to be important for review include a demonstrated knowledge of the applicable science, adequacy of facilities and commitment, availability of subject population when applicable and in-depth knowledge of the state-of-the-art to which the RFA is directed. The application will be judged upon the overall scientific merit, adequacy of methodology, facilities and resources, commitment of time and cost effectiveness of proposal, and quality of collaboration.

V. METHOD OF APPLYING

A. Format of Application

Applications must be submitted on form PHS 398, the application form for research project grants. Application kits are available at most institutional business offices, or may be obtained from the Division of Research Grants, NIH. The conventional presentation in format and detail applicable to regular research grant applications should be followed, and the requirements specified under Review Criteria (IV.B) must be fulfilled. Please check "Yes" in item 2 on the front page of your application, followed by the words "PROPOSAL IN RESPONSE TO RFA NIH-NCI-DCCP-SPB-82-11, BIOCHEMICAL EPIDEMIOLOGY."

B. Application Procedures

The completed original application and six (6) copies should be sent or delivered to:

Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205

To ensure their review, applications should be received by November 15, 1982. If applications are received after that date, the applicant will have the opportunity of having them considered in the next regular review cycle. Also, the Division of Research Grants (DRG) will not accept any application in response to this announcement, that is the same as one currently being considered by any other NIH awarding unit. Two copies of the application should also be sent to Dr. Copley at the address shown below.

VI. INQUIRIES

Inquiries may be directed to:

Dr. Genrose Copley
Special Programs Branch
Division of Cancer Cause and
Prevention
National Cancer Institute
Landow Building - Room 8C-16
Bethesda, Maryland 20205

Telephone: (301) 496-9600

REQUEST FOR RESEARCH GRANT APPLICATION: RFA

NIH-NCI-DCCP-SPB-82-12

"ACCURACY" OF QUESTIONNAIRE DERIVED HISTORIC DIETARY INFORMATION

NATIONAL CANCER INSTITUTE

Application Receipt Date: November 15, 1982

The Division of Cancer Cause and Prevention (DCCP) of the National Cancer Institute (NCI) invites grant applications from interested investigators for studies designed to investigate the "accuracy" and reproducibility of historical dietary information by comparing current information obtained by questioning individuals or their surrogates with actual records (data reflecting past dietary intake) of the same individuals recorded at some earlier point in time.

Grants are awarded to profit and nonprofit organizations and institutions, governments and their agencies, and occasionally to individuals. This type of grant solicitation (the RFA) is used to encourage investigator-initiated research projects in areas of special importance to the National Cancer Program. Applicants funded under the RFA are supported through the customary National Institutes of Health (NIH) grant-in-aid in accordance with Public Health Service (PHS) policies applicable to Research Project Grants including cost-sharing. The RFA solicitation, however, represents a single competition, with a specific deadline for receipt of applications. All applications received in response to the RFA are usually reviewed by the same NIH Initial Review Group (IRG). The specific deadline for the receipt of responses to this RFA is November 15, 1982. Applications should be prepared and submitted in accordance with the aims and requirements of the following sections:

I. BACKGROUND INFORMATION
II. OBJECTIVES AND SCOPE
III. MECHANISMS OF SUPPORT
IV. REVIEW PROCEDURES AND CRITERIA
V. METHOD OF APPLYING
VI. INQUIRIES

I. BACKGROUND INFORMATION

In chronic disease epidemiology in general, and cancer epidemiology in particular, the long intervals between exposures of interest and clinical onset of disease make studies of etiologic association extremely difficult. This problem is particularly acute in studies designed to investigate the initiating or modulating effects of past

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This program is described in the Catalog of Federal Domestic Assistance No. 13.393, Cancer Cause and Prevention Research. Awards are under authorization of the Public Health Service Act, Section 301(c) and Section 402 (Public Law 78-410, amended; 42 USC 241; 42 USC 282) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

nutritional exposures. Such investigations require that individuals attempt to mentally reconstruct their pattern of food consumption at some time in the past. In the rare event that the investigation is focused on some single dietary component (e.g., coffee consumption), it might be expected that recall would be reasonably accurate. In the usual situation, however, where the investigation requires that information be obtained on a much broader spectrum of dietary components, or even on the diet as a whole, it can be anticipated that recall will be much less accurate and will be affected by a variety of factors.

With the current emphasis on nutrition as a potential etiologic or modulating factor in human carcinogensis, it has become increasingly important to attempt an assessment of the degree to which dietary histories can be relied upon as substitutes for hard data on past food consumption or changes in dietary patterns. The recall period of interest to investigators in the cancer research area is likely to be years rather than months or weeks.

Useful information about the reliability of recall can be gained by comparing information obtained currently about previous diet with actual records of the dietary intake of the same individuals recorded at some discrete time in the past. In this context it must be stressed that no totally accurate methods for assessing dietary intake for non-institutionalized individuals currently exist. Even the maintenance of intake diaries or 24 hour recall methods do not provide totally accurate information on usual intake since bias may be introduced by a number of factors such as, for example, deliberate changes to simplify record-keeping or selective recall. This fact complicates our usage of the terms "validity" and "accuracy" for the purpose of this RFA and it must be remembered that the primary focus is on the value of historical dietary information as a predictor of cancer risk. The cancer epidemiologist needs information on how well historical dietary data separates individuals into low, middle and high consumers of a specific dietary component or food group. It would also be of interest to determine the "accuracy" of recall information from surrogate respondents since this procedure is often necessary in the conduct of studies in cancer epidemiology where the individual of concern is deceased or unable to respond adequately.

II. OBJECTIVES AND SCOPE

The primary objective of this RFA is to encourage studies aimed at assessing the accuracy and validity of historical dietary information obtained by questioning individuals or their surrogates. The elapsed time between the questioning and the dietary events of interest, for the purpose of this RFA, should be on the order of years rather than months or weeks. Variables, other than elapsed time, investigated in such studies might include: the age and sex of subjects, educational level, health status, complexity of questioning, dietary variability, and the effects of "out of home" food consumption. It might be desirable to assess the usefulness of special techniques to improve recall, validity of the original dietary data, its generalizeability and/or the availability of laboratory markers of past exposure.

Investigators responding to this RFA are encouraged to propose innovative approaches to data collection and analysis on methodology. The active involvement of persons experienced in the use of historical dietary information in the conduct and analysis of epidemiologic studies and access to appropriate historical dietary data are essential in responses to this application.

III. MECHANISM OF SUPPORT

The responses to this RFA will use the traditional NIH grant-in-aid. The RFA identifies the scope of the Institute's interest. It is expected that responsibility for the planning, direction and execution of the proposed research will be solely that of the applicant. The intent is to fund multiple projects with total costs amounting to approximately $300,000 for the first year. This funding level is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of the National Cancer Institute, the award of grants pursuant to this RFA is also contingent upon the availability of funds for this purpose.

This award may not be used to supplement support for an ongoing project.

IV. REVIEW PROCEDURES AND CRITERIA

A. Review Procedures

Each application submitted in response to the RFA will be reviewed by: (1) an appropriate initial peer review panel of the Division of Research Grants, National Institutes of Health, for scientific merit and (2) the National Cancer Advisory Board. All applications will be evaluated in competition with each other on a nationwide basis.

B. Review Criteria

Applications must be responsive to this RFA, in the sense of being directed toward the attainment of the stated programmatic goals. They will be considered in competition with each other for these RFA monies. If the application is judged by the National Cancer Institute not to be responsive, the applicant may have it considered as a traditional R01, along with other unsolicited applications in the next regular review cycle.

The factors considered in evaluating each response to this RFA will be:

1. Scientific merit of research approach, design, and methodology.

2. Research experience and competence of the Principal Investigator and staff in the use of historical dietary information in the conduct of the proposed studies.

3. Adequacy of time (effort) which the Principal Investigator and staff would devote to the proposed studies.

4. Adequacy of existing/proposed facilities and resources (including the availability of appropriate historical dietary data). Applications which specify a proposed use of human specimens need to provide assurance and details concerning the nature, source, and availability of those specimens.

V. METHODS OF APPLYING

A. Format of Application

Applications should be submitted on form PHS 398 (rev. 5/80), the application form for research project grants. Application kits are available at most institution business offices, or may be obtained from the Division of Research Grants, NIH. The conventional presentation in format and detail applicable to regular research grant applications should be followed, and the requirements specified under Review Criteria (IV.B) must be fulfilled. The words "PROPOSAL IN RESPONSE TO RFA NIH-NCI-DCCP-SPB-82-12 "ACCURACY" OF QUESTIONNAIRE DERIVED HISTORIC DIETARY INFORMATION" must be typed in bold letters across the face page of the application.

B. Application Procedure

The completed original application and six (6) copies should be sent or delivered to:

Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205

To ensure their review, applications should be received by November 15, 1982. If applications are received after that date, the applicant will have the opportunity of having them considered, along with other unsolicited applications, in the next regular review cycle. Also, the Division of Research Grants (DRG) will not accept any applications in response to this announcement which is the same as one currently being considered by any other NIH awarding unit. A copy of the application should be sent to Dr. Hjortland at the address shown below.

VI. INQUIRIES

Inquiries may be directed to:

Dr. Marthana C. Hjortland
Special Programs Branch
Division of Cancer Cause and Prevention
National Cancer Institute
Landow Building - Room 8C-18
Bethesda, Maryland 20205

Telephone: (301) 496-9600

PROGRAM RESEARCH INTERESTS IN IMMUNE MECHANISMS OF CUTANEOUS DISORDERS (IMMUNODERMATOLOGY)

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

The National Institute of Allergy and Infectious Diseases is interested in expanding research activities of the Immunology, Allergic and Immunologic Diseases Program concerned with immune mechanisms and hypersensitivity reactions in diseases of the skin. Investigations dealing with involvement of the skin as target tissue by immune humoral and cellular reactants and with cells of the integument serving as natural sources of specific antigens in immune processes are required to further our understanding of immunologic and allergic cutaneous diseases. The development of such studies will depend upon joint investigative endeavors in the disciplinary areas of allergy, dermatology, and immunology (immunobiology, immunochemistry, immunogenetics, and immunopharmacology).

The role of hypersensitivity and immune related inflammatory mechanisms in disorders of the skin as a product of both basic and clinical investigations has become increasingly evident. Additionally, the recognition of the common occurrence and socioeconomic impact of allergic skin diseases has provided the stimulus to further major efforts in relevant dermatology and allergy-immunology research at an increasing number of university sections and medical centers. Clinical immunologists are in a position to take advantage of the ready access of the skin for in vivo studies of both immune mechanisms in the production of local lesions and systemic immunopathologic processes with manifestations at cutaneous sites. The purpose of this announcement is to encourage the interaction of researchers in allergy, dermatology, and immunology in order to advance progress in the prevention, diagnosis, and treatment of immune-mediated skin diseases.

Some areas encompassed by the scope of this program include investigations designed to study allergic phenomena and immune mechanisms in the following conditions:

1. Studies to differentiate allergic skin disorders arising as a result of IgE related mechanisms: cell-mediated immunity/delayed hypersensitivity, and inflammation emerging from activation of the complement cascade and the effects of chemical mediators.

2. Atopic dermatitis: the definition of possible interacting etiologies that influence the development and course of allergic eczema as a multifactorial disorder.

3. Urticaria and angioedema: investigations to detect and define the multiple allergenic, neurogenic, chemical, and microcirculatory factors that result in heterogeneous disorders with identical presentation.

This program is described in the Catalog of Federal Domestic Assistance No. 13.855, Immunology, Allergic and Immunologic Diseases Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

4. Contact hypersensitivity: evaluation of the nature of normal skin cell components converted to antigenic determinants as a result of interaction with sensitizing agents.

5. Infection: immune responses to both pathogenetic and saprophytic flora serving as microbial antigens in immune and hypersensitivity reactions.

METHOD AND CRITERIA FOR REVIEW

Assignment of Application

Applications will be received by the NIH Division of Research Grants, referred to an appropriate study section for scientific review, and assigned to the NIAID for possible funding, unless programmatic considerations indicate more appropriate assignment to an alternative awarding unit. These decisions will be governed by normal programmatic considerations as specified in the DRG referral Guidelines.

Review Procedures

Applications in response to this announcement will be reviewed on a nationwide basis in competition with each other, and in accord with the usual National Institutes of Health peer review procedures. They will first be reviewed for scientific and technical merit by a review group composed mostly of non-Federal scientific consultants (study section). Following study section review, the application will be evaluated for program relevance by the NIAID Advisory Council. The review criteria customarily employed by the National Institutes of Health for regular research grant applications will prevail.

Deadline

Applications will be accepted in accordance with the usual receipt dates for new applications:

March 1 July 1 November 1

Method of Applying

Applications should be submitted on form PHS 398 (Rev. 5/80) which is available in the institution's business office. If not available there, they may be obtained from:

Office of Grants Inquiries
Division of Research Grants
National Institutes of Health
Westwood Building - Room 448
Bethesda, Maryland 20205

The phrase "PREPARED IN RESPONSE TO PROGRAM RESEARCH INTERESTS IN IMMUNE MECHANISMS AND CUTANEOUS DISORDERS (IMMUNODERMATOLOGY)" should be typed across the top of the first page of the application.

The original and six copies of the application should be sent or delivered to:

Application Receipt Office
Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
Bethesda, Maryland 20205

For further information investigators are encouraged to contact:

Robert A. Goldstein, M.D., Ph.D.
Chief, Allergy and Clinical
Immunology Branch
National Institute of Allergy and
Infectious Diseases
Westwood Building - Room 755
Bethesda, Maryland 20205

Telephone: (301) 496-7104

In order to alert the Skin Diseases Program of the NIADDK to the submission of proposals with primary thrust directed to dermatology, you may wish to communicate with:

Alan N. Moshell, M.D.
Director, Skin Diseases Program
Extramural Programs
National Institute of Arthritis, Diabetes,
and Digestive and Kidney Diseases
Westwood Building - Room 405
Bethesda, Maryland 20205

Telephone: (301) 496-7326

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA NIH-NIAID-82-9

PROGRAM PROJECTS IN LYMPHOCYTE BIOLOGY

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Application Receipt Date: February 15, 1983

I. BACKGROUND INFORMATION

The Immunobiology and Immunochemistry Branch of the Immunology, Allergic and Immunologic Diseases Program of the NIAID supports fundamental studies on the structure and function of the immune system to gain an understanding of immune response mechanisms at their basic cellular and molecular levels as they function in health and disease. Program Projects in Lymphocyte Biology represent an award mechanism which the Branch has employed to meet this objective. Each program project utilizes an integrated multidisciplinary approach for basic biologic studies of immunologically-functional lymphocyte populations. Five such program projects are now supported although support for one is scheduled to conclude in 1984. This request for applications (RFA) is intended to encourage the development of proposals from collaborating investigators and to coordinate the submission and review of new and renewal program project applications, providing an equitable opportunity for both to compete for funds currently available to the Program in this area of research.

II. RESEARCH GOALS AND SCOPE

The ultimate goal of these program projects is the attainment of a complete knowledge of the life history of immunocompetent cells and of the genetic and phenotypic factors that determine their fate and function in vivo and in vitro. The ultimate practical application would be the use of selected cloned lymphocytic cells and their products for the clinical care or reconstitution of immunodeficient individuals, to alleviate allergic states, to provide resistance to life-threatening infections and to correct aberrant or defective immunoregulatory mechanisms.

The scope of these program projects includes studies of every facet of the immune response ranging from the initial step of antigen recognition to the final elaboration of immunologically distinctive products of specific lymphocytes. Research currently supported by this mechanism was designed to greatly expand knowledge of the morphologic and functional heterogeneity of lymphocyte populations and to develop the capability for identification and selection of

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This program is described in the Catalog of Federal Domestic Assistance No. 13.855, Immunology, Allergic and Immunologic Diseases Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency Review.

lymphocyte subpopulations with specific immune reactivity or antigenic composition, for hybridization of such populations and for selective production of specific, biologically-active, lymphocyte products.

Proposals submitted in response to this RFA should consist of a number of integrated component projects utilizing multifaceted experimental approaches and the technical expertise of cell biologists, cellular immunologists, immunochemists, microbiologists, and geneticists. However, the proposal should clearly explain how the planned multidisciplinary approach can be expected to accomplish the stated goal more efficiently and effectively than a series of independent individual grant-supported studies.

Proposals should emphasize new ideas and new initiatives and should be concerned with the acquisition of new knowledge relevant to the immune system and its structure and function. Although proposals are expected to be based primarily on experimental laboratory investigations, the value and place of clinical studies are recognized. Inclusion of patient oriented studies or laboratory procedures utilizing human source materials is acceptable, provided such studies have an immunologic base or draw upon immunologically relevant technology.

Designation of an individual to serve as the program project director should be based upon accomplishment, experience as a senior scientist and ability to assume both leadership of the investigative group and responsibility for scientific, professional, and administrative functions, and commitment of a significant amount of time to the project. Each component project in the proposal should have a designated principal investigator, also with a demonstrable record of accomplishment in one of the basic science disciplines or clinical specialties relevant to the particular subject of investigation.

III. MECHANISM OF SUPPORT

Program project grants are awarded to an institution in behalf of a program director for the support of a broadly based, multidisciplinary, long-term research program which has a specific major objective or basic theme. A program project generally involves the organized efforts of groups of investigators, members of which conduct research projects related to the overall program objective. The grant can provide support for the projects and for certain core resources shared by individuals in a program where the sharing facilitates the total research effort. Each component project supported under a program project grant is expected to contribute to and be directly related to a common theme; the projects should demonstrate an essential element of unity and interdependence.

This program does not provide support for nonresearch components, such as a clinical referral service or a clinical laboratory service function.

Grant funds may be utilized to support the research activities of scientific and professional personnel, administration, consultation services, central support services, equipment, supplies, travel, and publications costs. Support for research-related cost of patient involvement and medical care may be authorized. Since the Program cannot provide funds for new construction, adequate physical facilities must be available for the primary needs of the project. However, moderate alterations or renovations to enhance clinical or laboratory facilities may be allowed if they are necessary to meet objectives of the proposal.

Support of a program project in Lymphocyte Biology will be limited to a maximum of five years. If a competing renewal application is planned, it should be submitted only in response to an RFA. Funding beyond the first and subsequent years of the grant will be contingent upon satisfactory progress during the preceding years.

IV. REVIEW PROCEDURES AND CRITERIA

The receipt date for applications will be February 15, 1983. They will undergo initial review in June by the Transplantation Biology and Immunology Subcommittee and subsequent review by the National Advisory Allergy and Infectious Diseases Council in October 1983. It is planned that at least one program project grant award will be made during fiscal year 1984 depending on the availability of funds. May 1, 1984, will be the earliest starting date for successful applicants.

Prospective program directors are strongly encouraged to submit a "letter of intent" for preliminary screening by NIAID Staff. Letters of intent should cover the following points.

1. A brief description of the intended project.
2. A description of available laboratory and clinical facilities.
3. Ongoing relevant research studies, identifying existing projects and sources of support.
4. Past research by members of the proposed investigative group relevant to the proposal.
5. The academic positions and major research interests of the program director and his professional staff who will be involved in the proposed studies.
6. Collaborative arrangements with other area laboratories and investigator and delineation of the roles and manner of anticipated participation and interaction of the principal investigators, consultants, and collaborators.

Letters of intent are due no later than November 15, 1982, and upon receipt will be screened by NIAID Staff to determine the eligibility and suitability of the project proposals for this announcement.

Inquiries should be directed to:

Bernard W. Janicki, Ph.D.
Chief, Immunobiology and Immunochemistry
Branch, IAIDP
National Institute of Allergy and
Infectious Diseases
National Institutes of Health
Westwood Building - Room 757
Bethesda, Maryland 20205

Telephone: (301) 496-7551

V. CONSEQUENCES OF LACK OF RESPONSIVENESS TO THE RFA OR OF LATE SUBMISSION

Based on the letter of intent, potential applicants will be promptly advised whether or not their proposal is found to be within the research goals and scope of the program as defined in the RFA. Applicants will then have an opportunity to correct deficiencies or weaknesses and to restructure their submissions accordingly. Formal applications that are not responsive to the RFA or are not received by February 15, 1983, will not be accepted for review and will be returned to the applicant.

VI. METHOD OF APPLYING

Before preparing an application, the prospective applicant should request a copy of the NIAID Information Brochure on Program Projects from:

Dr. Nirmal Das
Executive Secretary
Allergy, Immunology and Transplantation
Research Committee
National Institute of Allergy and
Infectious Diseases
National Institutes of Health
Westwood Building - Room 706
Bethesda, Maryland 20205

Telephone: (301) 496-7966

In order to assure adequate review it is important to follow instructions in the Information Brochure, which contains details on the format and requirements for multidisciplinary grant applications.

Use the standard research grant application form PHS 398 (Rev. 5/80) In addition to following accompanying format instructions for the development of the application, include expanded material listed above for the letter of intent. For purposes of identification and processing, the words "PROGRAM PROJECT IN LYMPHOCYTE BIOLOGY" should be typed in item 2 on the face page of the application and a brief covering letter should be attached indicating submission is in response to this NIAID announcement.

Application kits may be obtained from the institution's application control office. If not available there, they may be obtained from:

Office of Grants Inquires
Division of Research Grants
National Institutes of Health
Westwood Building - Room 448
Bethesda, Maryland 20205

Forward the original application and six (6) copies to:

Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
Bethesda, Maryland 20205

In order to alert NIAID to the submission of the proposal, please forward a copy (not the original) of the cover letter and the application face page to the following:

Chief, Program and Project Review Branch
National Institute of Allergy and
Infectious Diseases
National Institutes of Health
Westwood Building - Room 703
Bethesda, Maryland 20205.

REQUEST FOR RESEARCH GRANT APPLICATION: RFA

NIH-NCI-DCCP-SPB 82-14

THE PHARMACOLOGICAL ROLE OF NICOTINE IN DISEASES RELATED TO TOBACCO PRODUCTS

NATIONAL CANCER INSTITUTE

Application Receipt Date: November 1, 1982

The Division of Cancer Cause and Prevention (DCCP) of the National Cancer Institute (NCI) invites grant applications from interested investigators to investigate the pharmacological role and biological effects of nicotine related to tobacco product carcinogenesis.

Grants are awarded to organizations and institutions, governments and their agencies, and occasionally to individuals. This type of grant solicitation (the RFA) is utilized when it is desired to encourage investigator-initiated research projects in areas of special importance to the National Cancer Program. Applicants funded under the RFA are supported through the customary NIH grant-in-aid in accordance with PHS policies applicable to Research Project Grants including cost-sharing. All applications received in response to the RFA will be reviewed by an NIH Division of Research Grants (DRG) review group.

The present RFA announcement is for a single competition with a specified deadline of November 1, 1982 for receipt of applications. Applications should be prepared and submitted in accordance with the aims and requirements described in the following sections:

I. BACKGROUND INFORMATION
II. OBJECTIVE AND SCOPE
III. MECHANISM OF SUPPORT
IV. REVIEW PROCEDURES AND CRITERIA
V. METHOD OF APPLYING
VI. INQUIRIES

I. BACKGROUND

Past studies have shown nicotine to be the only controlled variable in tobacco smoke condensate which is consistently related to the rate of tumor incidence in test animals. However, in separate studies, nicotine itself has not been shown to be

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This program is described in the Catalog of Federal Domestic Assistance No. 13.393, Cancer Cause and Prevention. Awards will be made under the authority of the Public Health Service Act, Section 301(c) and Section 402, Public Law 78-410, as amended; (42 U.S.C. 241 and 282) and administered under PHS grant policies and Federal regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

a carcinogen. It has been noted that the relationship between carcinogenic activity of smoke condensates and their nicotine contents may be caused in part by the conversion of nicotine to tobacco-specific nitrosamines or to the co-occurrence of nicotine and some other carcinogen or cocarcinogen. Tobacco products made from the lamina of plants grown on high levels of nitrate fertilizer contain higher levels of nicotine and following combustion show higher levels of volatile nitrosamines.

The exact role of nicotine, its metabolic and pyrolytic products, needs to be clarified in relation to carcinogenesis associated with tobacco smoke inhalation. Such information would be applicable in evaluating health effects produced by smoking tobacco products having various tar/nicotine ratios.

II. OBJECTIVE AND SCOPE

The primary objective of this RFA is to define the pharmacological role of nicotine in selected animal model(s), or humans, exposed to cigarette smoke under chronic conditions. The proposed work should address precursor states which have indications of being related to cigarette smoke carcinogenesis in animals and/or humans. These may include markers in body fluids or organ specific markers which may be demonstrated by immunological, histochemical, biochemical or other functional indices with the objective being to characterize and quantify different degrees of response and/or injury associated with exposure to nicotine, its metabolites or selected cofactors. The proposed studies should not be planned as merely screening tests, but should have a rationale based on previous findings described in peer-reviewed publications.

To maximize the findings of the investigations in regard to the role of nicotine and other selected components, the inhalation experiments must be planned so that valid comparisons may be made both in regard to dosimetry and end point observations.

Applications which propose studies with the use of human subjects must be in compliance with 45 Code of Federal Regulations 46 (Revised 01/26/81).

III. MECHANISM OF SUPPORT

This RFA will use the traditional National Institutes of Health grant-in-aid. Responsibility for the planning, direction, and execution of the proposed research will be that of the applicant. The duration for applications submitted in response to this RFA should not exceed five years. The intent is to fund multiple projects with total costs amounting to approximately $350,000 for the first year. This funding level is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plan of the National Cancer Institute, the award of grants pursuant to this RFA is contingent upon the availability of funds for this purpose.

IV. REVIEW PROCEDURES AND CRITERIA

A. Review Method

All applications submitted in response to this RFA will be reviewed by: (1) a review group of the Division of Research Grants, NIH; and (2) the National Cancer Advisory Board. All applications will be evaluated on a competitive basis.

B. Review Criteria

Applications must be responsive to this RFA, in the sense of being directed toward the attainment of the stated programmatic objective. If the application is judged by the National Cancer Institute not to be responsive to the RFA, the applicant will have the opportunity of having his application considered along with other unsolicited applications received by the National Institutes of Health in the review cycle which is current at that time.

The factors to be considered in evaluating the proposals which are responsive to this RFA are:

1. Scientific merit of proposed research, design and methodology.
2. Research experience and competence of the Principal Investigator and staff.
3. Availability and adequacy of time which the Principal Investigator and staff would devote to the proposed studies.
4. Adequacy of existing/proposed facilities and resources.
5. Probability of the investigator obtaining goals which are set forth in the application.

V. METHODS OF APPLYING

Applications should be submitted on form PHS 398, which is available at most institutional business offices, or may be obtained from the Division of Research Grants, NIH. The words "Proposal in response to RFA: PHARMACOLOGICAL ROLE OF NICOTINE IN DISEASES RELATED TO TOBACCO PRODUCTS" must be typed in bold letters across the top of the front page of the application.

The completed original application and six copies should be sent or delivered to:

Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205

Applications must be received by the National Institutes of Health by November 1, 1982. The Division of Research Grants (DRG) will not accept any application in response to this announcement that is the same as one currently being considered by any other NIH awarding unit. A copy of the application should also be sent to Dr. Thomas B. Owen at the address shown below, and a copy to the following:

Dr. Harold Waters
Chief, Special Review Section
Division of Research Grants
Westwood Building - Room 2A16
Bethesda, Maryland 20205

VI. INQUIRIES

Inquiries may be directed to:

Dr. Thomas B. Owen
Special Programs Branch
Division of Cancer Cause
and Prevention
National Cancer Institute
Landow Building - Room 8C18
Bethesda, Maryland 20205

Telephone: (301) 496-9600

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

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HAVE YOU MOVED?

If your present address differs from that shown on the address label, please send your new address to: Grants and Contract Guide Distribution Center, National Institutes of Health, Room B3BN10, Building 31, Bethesda, Maryland 20205, and attach your address label to your letter. Prompt notice of your change of address will prevent your name from being removed from our mailing list.

The GUIDE *is published at irregular intervals to announce scientific initiatives and to provide policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in grants and contracts activities administered by the National Institutes of Health.*

Two types of supplements are published by the respective awarding units. Those printed on yellow paper concern contracts: solicitations of sources and announcement of availability of requests for proposals. Those printed on blue paper concern invitations for grant applications in well-defined scientific areas to accomplish specific program purposes.

HE20.3008/2:

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NOTICE

TERMINATION OF GERIATRIC DENTISTRY ACADEMIC AWARD

The National Institute on Aging (NIA) announces that, effective immediately, no further applications for the Geriatric Dentistry Academic Award will be accepted by the Institute.

Existing Geriatric Dentistry Academic Awards are in no way affected by this announcement and will be funded by NIA through their expected termination dates at the end of the fifth year.

Those applications for the Geriatric Dentistry Academic Award which were received by the NIH Division of Research Grants to meet the annual receipt date of July 1, 1982, will be processed, reviewed for scientific merit, and a funding decision reached.

ANNOUNCEMENT

INFORMATION STATEMENT ON ALEXANDER VON HUMBOLDT FOUNDATION POSTDOCTORAL RESEARCH FELLOWSHIPS FOR 1982-83

FOGARTY INTERNATIONAL CENTER

The Fogarty International Center of the National Institutes of Health announces the sponsorship of research fellowships for 1982-83 by the Alexander von Humboldt (AvH) Foundation of the Federal Republic of Germany. These fellowships will be awarded to qualified biomedical scientists for the purpose of providing research experiences and training at the postdoctoral level in basic or clinical sciences related to health in the Federal Republic of Germany.

To be eligible, candidates must have an earned degree of Ph.D., M.D., D.V.M., D.D.S., or an equivalent degree, and must have been engaged in independent research in one of the health sciences for at least two of the last four years. The fellowships are intended in principle for scientists in the formative stages of their research careers. The formative stage is generally defined as having less than five years of postdoctoral experience and the applicant being less than 38 years of age.

Applicants must present evidence of aptitude and promise in basic biomedical or clinical research, with an active interest in pursuing a research career in a health science field. This evidence must be presented in the form of a scientific bibliography, a precise research proposal, copies of reprints, and references from individuals familiar with the applicant's background, ability, and promise for a research career.

Applicants must also provide evidence of acceptance by a training institution and preceptor in the Federal Republic of Germany. It is the applicant's responsibility to arrange for his or her research training with the preceptor. Arrangements may be made either through direct correspondence between the applicant and a scientist in the Federal Republic of Germany, or through correspondence initiated on the applicant's behalf by a senior scientist in the United States with a German colleague. It is expected that such correspondence will lead to the development of a plan for original research which will be worked out by the applicant himself and presented clearly in the application. The acceptance is documented by a letter of invitation which is a requisite part of the application and without which no application will be considered.

Applications are considered by the Selection Committee of the AvH Foundation. This committee is composed of 95 German scholars of all disciplines and takes decisions exclusively on the basis of academic merit and achievement. It is not bound by quotas, in respect of either countries or academic disciplines.

Consideration of applications takes several months. The Selection Committee of the AvH Foundation meets three times a year, usually in March, July, and November. The AvH Foundation recommends that the complete application should reach the Foundation's Office in Bonn five months before the committee meeting at the latest. The processing of incomplete applications will be considerably delayed.

The starting date of the fellowship will be set by mutual agreement between the applicant and the preceptor or host institution, provided it is in general within the 12 month period immediately following the date of the award and approved by the Foundation. The fellowship will normally extend for 12 months after the starting date, but an extension of up to 12 months may be considered, if recommended by the host institution and approved by the AvH Foundation.

Fellowships range from DM 2.100 to DM 2.900 per month, the level depending upon the number of years of postdoctoral experience of the applicant at the time of award. There are additional provisions for covering spouse and children, travel expenses, German language courses, etc. Group health insurance is available at reasonable rates, at present DM 64 per month for men, DM 105 per month for women.

Application forms may be submitted to the Alexander von Humboldt Foundation at any time of the year. Individuals interested in applying for this fellowship should request the latest Information Sheet and application forms from:

International Research Fellowship Programs
Fogarty International Center
National Institutes of Health
Building 38A - Room 613
Bethesda, Maryland 20205

or directly from:

Alexander von Humboldt Stiftung
Bad Godesberg
- Auswahlabteilung -
Jean-Paul-Strabe 12
D - 5300 Bonn 2
Federal Republic of Germany

ANNOUNCEMENT

ONCOGENE PRODUCTS IN IRRADIATED CELLS AND TISSUES

NATIONAL CANCER INSTITUTE

The National Cancer Institute's (NCI) Division of Cancer Treatment (DCT) desires to expand its support of radiation effects research. The program is seeking applications for research grants concerned with testing the hypothesis that oncogene expression occurs as a step in radiation induction of some tumors. Experiments are to be designed to detect the presence of oncogene products in irradiated cells or tissues that convert to malignant behavior in vitro and/or in vivo. Methods to be used may include, but need not be limited to, the use of immunocytochemical markers or cDNA probes. Although it is expected that emphasis will be placed on experiments that seek retrovirus gene products, tumor antigens thought to be produced by certain DNA viruses may also be sought. Any biological test system may be used for study, but the ultimate goals of the program would benefit greatly from the study of human cells. In making this program announcement, it is not the intent of the National Cancer Institute to make or imply any delimitation of research related to oncogene expression, but rather to stimulate investigator-initiated research in this particular field.

Applications in response to this announcement will be reviewed on a nationwide basis in competition with each other, and in accord with the usual National Institutes of Health (NIH) peer review procedures. They will first be reviewed for scientific and technical merit by a review group composed mostly of non-federal scientific consultants. Following this initial review, the application will be evaluated for program relevance by the National Cancer Board. The review criteria customarily employed by the NIH for regular research grant applications will prevail. Applications will be accepted in accordance with the usual NIH receipt dates for new applications: March 1, July 1, and November 1.

METHOD OF APPLYING

Applicantions should be submitted on form PHS-398, which is available in the grants and contracts business office at most academic and research institutions or from the Division of Research Grants, NIH. The title of this Program Announcement should be typed in section 2 on the front page of the grant application form.

This program is described in the Catalog of Federal Domestic Assistance No. 13.395, Cancer Treatment Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

In addition, a brief covering letter should accompany the application indicating it is being submitted in response to this program announcement. The original and six copies of the application should be sent or delivered to:

Applications Receipt Office
Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
Bethesda, Maryland 20205

For further information, investigators are encouraged to contact:

Dr. James L. Murray
Low-Level Radiation Effects Branch
Division of Cancer Treatment
National Cancer Institute
Building 31 - Room 4B29
Bethesda, Maryland 20205

Telephone: (301) 496-9326

In order to alert the Division of Cancer Treatment to the submission of proposals with primary thrust directed to radiation effects research, a copy of the covering letter should be sent to Dr. Murray.

PROGRAM ANNOUNCEMENT

SPECIFIC RADIATION-INDUCED CHROMOSOMAL ABNORMALITIES AND CANCER

NATIONAL CANCER INSTITUTE

The National Cancer Institute's Division of Cancer Treatment desires to expand its support of radiation effects research. The program is seeking applications for research grants for basic studies to answer questions concerning the relationship between radiation-induced chromosomal translocations and radiation-induced cancer. For example, are specific translocations found in recently-transformed irradiated cells; do radiation-induced animal tumors consistently contain cells that are nearly euploid but contain specific translocations; and can evidence be found for chromosomal abnormalities as an etiologic factor in human radiogenic tumors? In making this program announcement, it is not the intent of the National Cancer Institute to make or imply any delimitation of research related to chromosomal abnormalities, but rather to stimulate investigator-initiated research in this particular field.

Studies to be proposed should consider promising areas of research using cytogenetic methods in experiments involving *in vitro* cell transformation, animal tumor induction, or putative radiogenic cancers in human patients. Experimental plans should clearly identify the biological system(s) to be used, criteria for malignancy to be applied, and cytogenetic procedures to be utilized. Because one of the most likely cytogenetic end-points to be assayed is the unbalanced translocation, it is expected that chromosome banding procedures, with quantitative measurements if necessary, will be used in the cytogenetic aspects of the study. The use of a particular biological system should be justified on the basis of its potential for simultaneous cytogenetic study in carcinogenesis experiments.

Applications in response to this announcement will be reviewed on a nationwide basis in competition with each other, and in accord with the usual National Institutes of Health peer review procedures. They will first be reviewed for scientific and technical merit by a review group composed mostly of non-federal scientific consultants. Following this initial review, the application will be evaluated for program relevance by the National Cancer Advisory Board. The review criteria customarily employed by the National

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This program is described in the Catalog of Federal Domestic Assistance No. 13.395, Cancer Treatment Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

Institutes of Health for regular research grant applications will prevail. Applications will be accepted in accordance with the usual NIH receipt dates for new applications: March 1, July 1, and November 1.

METHOD OF APPLYING

Applications should be submitted on form PHS-398, which is available in the grants and contracts business office at most academic and research institutions or from the Division of Research Grants, NIH. The title of the RFA program announcement should be typed in section 2 on the front page of the grant application form.

In addition, a brief covering letter should accompany the application indicating it is being submitted in response to this program announcement. The original and six copies of the application should be sent or delivered to:

Applications Receipt Office
Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
Bethesda, Maryland 20205

For further information, investigators are encouraged to contact:

Dr. James L. Murray
Low-Level Radiation Effects Branch
Division of Cancer Treatment
National Cancer Institute
Building 31 - Room 4B29
Bethesda, Maryland 20205

Telephone: (301) 496-9326

In order to alert the Division of Cancer Treatment to the submission of proposals with primary thrust directed to radiation effects research, a copy of the covering letter should be sent to Dr. Murray.

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

NIH-NCI-DCT-LLREB-82-15

CARCINOGENESIS IN SMALL ANIMALS IRRADIATED IN UTERO

NATIONAL CANCER INSTITUTE

Application Receipt Date: December 1, 1982

The Division of Cancer Treatment of the National Cancer Institute (NCI) invites grant applications from interested investigators for basic studies to measure the carcinogenic effects of low levels of ionizing radiation on the developing embryo and fetus in small animals.

This type of grant solicitation (the RFA) is utilized when it is desired to encourage investigator-initiated research projects in areas of special importance to the National Cancer Program. Applicants funded under the RFA are supported through the customary National Institutes of Health (NIH) grant-in-aid, in accordance with PHS policies applicable to Research Project Grants including cost sharing. However, the RFA solicitation represents a single competition, with a specified deadline for receipt of applications. All applications received in response to the RFA will be reviewed by the same NIH Initial Review Group.

The present RFA announcement is for a single competition with a specified deadline of December 1, 1982 for receipt of applications. Applications should be prepared and submitted in accordance with the aims and requirements described in the following sections:

I. Background Information
II. Objective and Scope
III. Mechanism of Support
IV. Review Procedures and Criteria
V. Method of Applying
VI. Inquiries

I. BACKGROUND INFORMATION

The Low-Level Radiation Effects Branch (LLREB) of the Radiation Research Program, NCI, has as its major interest the effects of low levels of ionizing

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This program is described in the Catalog of Federal Domestic Assistance No. 13.395, Cancer Treatment Research. Awards are made under authorization of the Public Health Service Act, Section 301(c) and Section 402 (Public Law 78-410, as amended; 42 USC 241; 42 USC 282) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

radiation on biological systems. For the purposes of the LLREB, low-level is defined as acute exposures less than 10 rad. The major radiation effects occuring at these doses are mutagenesis, carcinogenesis, and in utero effects. LLREB has specific interests in each of these low-level effects including the influence of dose rate and LET.

Each year thousands of women are given radiodiagnostic examinations of the abdomen during pregnancy. The effects of these small doses of radiation on the developing embryo/fetus are a matter of controversy. Several human studies suggest that doses of 1-2 rad may increase the postnatal cancer risk; however, other epidemiologic studies have not confirmed this. Factors such as gestational age at time of exposure and maternal health status are likewise not well understood. Clearly, the risks of radiation exposure during pregnancy must be more clearly defined in order to facilitate benefit/risk decision-making in clinical practice.

This RFA is responsive to the Congressional mandate under the Biological Research Extension Act of 1978 (P.L. 95-622) as well as to the recommendations of the Interagency Radiation Research Committee's Federal Strategy for Research into the Biological Effects of Ionizing Radiation (June, 1981).

II. OBJECTIVE AND SCOPE

The carcinogenic effects of low levels of ionizing radiation on the developing embryo and fetus in small animals are to be measured in order to define the risks of radiation exposure during development. Any small laboratory animal system may be used. Single cell, tissue and organ systems may also be used where appropriate, such as in investigations of mechanisms of radiation effects in utero. Proposed studies should evaluate cancer induction in small animals following a wide range of radiation doses, including low doses. Factors influencing cancer induction such as gestational age at exposure, maternal health and endocrine status should also be considered in the study design. Other factors which may be studied include dose rate and LET. Analysis of the data may include dose response curves at low doses and comparison of the types of tumors produced.

III. MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health grant-in-aid. Responsibility for the planning, direction, and execution of the proposed research will be solely that of the applicant. The total project period for applications submitted in response to the present RFA should not exceed five years. The intent is to fund several projects, with total program costs amounting to approximately $400,000 for the first year. This funding level is dependent on the receipt of a sufficient number of applications of high scientific merit. Also, although this program is provided for in the financial plans of the NCI, the award of grants pursuant to this RFA is contingent upon the availability of funds for this purpose.

IV. REVIEW PROCEDURES AND CRITERIA

A. Review Method

Each application submitted in response to the RFA will be reviewed by: (1) an appropriate review group of the Division of Research Grants, NIH, and (2) the National Cancer Advisory Board.

Future renewal applications will not compete for earmarked funds. Instead, all renewal applications will be considered as unsolicited grant applications which will compete with all other unsolicited applications received by the NIH.

The factors considered in evaluating such response to this RFA will be:

1. Scientific merit of research approach, design, and methodology.
2. Research experience and competence of the Principal Investigator and staff to conduct the proposed studies.
3. Adequacy of time (effort) which the Principal Investigator and staff would devote to the proposed studies.
4. Adequacy of existing/proposed facilities and resources.
5. Scientific, technical or medical significance and originality of proposed research.
6. Reasonableness of proposed costs.

V. METHOD OF APPLYING

A. Format of Applications

Applications must be submitted on form PHS 398 (Revised 5/80), the application form for research project grants. Application kits are available at most institutional business offices, or may be obtained from the Division of Research Grants, NIH. The conventional presentation in format and detail applicable to regular research grant applications should be followed, and the requirements specified under Review Criteria (IV. B.) must be fulfilled. The number and title of this RFA should be typed in section 2 on the front page of the grant application form.

B. Application Procedure

The completed original application and six (6) copies should be sent or delivered to:

Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205

To ensure their review, applications must be received by December 1, 1982.

Applications received after that date will be returned. Also, the Division of Research Grants (DRG) will not accept any application in response to this announcement that is the same as one currently being considered by any other NIH awarding unit. One copy of this application should also be sent to each of the following individuals:

Dr. Harold Waters
Division of Research Grants
National Institutes of Health
Westwood Building - Room 2A16
Bethesda, Maryland 20205 and

Dr. James L. Murray, Low-Level Radiation Effects Branch
at the address shown below.

VI. INQUIRIES MAY BE DIRECTED TO:

Dr. James L. Murray
Low-Level Radiation Effects Branch
Division of Cancer Treatment
National Cancer Institute
Building 31, Room 4B29
Bethesda, Maryland 20205

Telephone: (301) 496-9326

REQUEST FOR RESEARCH GRANT APPLICATIONS:

RFA-NIOSH-82-2

PROTECTION FROM AIRBORNE TOXIC AND CARCINOGENIC MATERIALS BY RESPIRATORY PROTECTION SYSTEMS

CENTERS FOR DISEASE CONTROL

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH

Application Receipt Date: November 1, 1982

The National Institute for Occupational Safety and Health (NIOSH) announces that competitive grant applications for basic and applied research and demonstration projects to increase protection from airborne toxic materials and carcinogens by respiratory protection systems will be accepted until November 1, 1982.

I. BACKGROUND

The hazards of inhalation of carcinogens and other toxicants are a major concern for the modern worker. Recent concerns over carcinogens, such as vinyl chloride, asbestos, benzene, kepone, and other toxicants have focused on their inhalation hazards and necessary control technology. Clearly, engineering and administrative controls, such as improved ventilation, process changes, and good work practices, are the preferred approaches to protecting the worker from exposure to airborne toxic materials and carcinogens. However, the use of respirators is the only immediate option for situations in which engineering controls are not feasible or not yet available. The same may be true during the installation of engineering controls and during life-threatening emergency situations. In addition, respirators are frequently needed to supplement inadequate engineering controls. Unfortunately, respirators may not meet the needs of the workplace.

This program is described in the Catalog of Federal Domestic Assistance No. 13.262, Occupational Safety and Health Research Grants. These grants will be awarded and administered by NIOSH under the legislative authorization in section 20(a)(1) of the Occupational Safety and Health Act of 1970 (29 U.S.C. 669(a)(1) and section 501 of the Federal Mine Safety and Health Act of 1977 (30 U.S.C. 951). Program regulations applicable to these grants are in Part 87 of Title 42, Code of Federal Regulations, "National Institute for Occupational Safety and Health Research and Demonstration Grants." This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

NIOSH responsibilities include testing and certifying all types of industrial respirators; a field in which the Federal Government has been involved for more than 60 years. NIOSH has a fundamental responsibility to develop and maintain a modern certification program, advance the state of the art, and provide leadership in the respiratory protection field. It has become increasingly clear in recent years that respirator protection for workers is in need of significant improvement. Sparse research has been conducted in this field. Federal standards, originally intended only to evaluate respirators worn by miners, have not evolved into criteria adequate for evaluating respirators used in all work environments where airborne carcinogens are present.

Studies performed by NIOSH and others have confirmed that workers in many industries are not wearing the respirators that "go with the job." Workers claim that respirators are uncomfortable to wear. Whether the problem is heat buildup, strap headache, irritations behind the ears and over the jaw, ingrown hairs, inflamed sweat glands, dehydration, poor fit, difficulty in speech transmission, visibility limitation, or other problems, many workers do not wear existing respirators for extended periods of time. NIOSH believes, based on available data and the opinions of some of the nation's leading respirator experts, that the problem is one of basic design--existing respirators are not amenable to wearing for extended periods of time.

II. ELIGIBLE APPLICANTS

Eligible applicants may be universities, colleges, research institutions and other public and private organizations including State and local governments. Note that for-profit institutions are now eligible for research and demonstration grants.

III. AVAILABLE FUNDS

The annual amount available for grants under this announcement will be between $400,000 and $600,000. Award of grants is contingent upon availability of funds for this purpose and successful peer review, including priority ranking. Grantees will be required to cost share a minimum of 5 percent. Grants may be supported for up to 5 years, and may be renewed for an additional period, subject to the competitive review procedure and availability of funds for this announcement.

IV. AREAS OF RESEARCH INTEREST

A. The goal of this announcement is to stimulate and encourge high quality research and demonstration grants in the areas listed below. These areas are not mutually exclusive. It is anticipated that a given research study may cut across several areas. Included under each listed area are examples of the types of studies which would be of interest to NIOSH. They are not meant to be restrictive and are cited for illustrative purposes only:

1. Engineering:

   a. Development of new and innovative respiratory protective devices.

   b. Development of a positive, general, end-of-service-life indicator for sorbents of air purifying respirators.

   c. Research and development of test techniques and models to predict general respirator performance as well as component performance against heat, radiant heat, chemical attack, shock, vibration, etc.

   d. Development of an inexpensive, universal facepiece fit tester.

   e. Studies of methods to increase effective protection factors in the field under actual workplace conditions.

2. Industrial Hygiene:

   a. Studies to evaluate the effectiveness of established respirator programs. Such studies may measure effective protection factors and develop techniques for improving long-term respiratory protection.

   b. Studies to define those factors of a respiratory protection program which influence worker acceptance and continued proper use of respirators.

   c. Studies to evaluate the significance of worker participation in respirator programs, including selection and maintenance.

   d. Studies to evaluate respiratory protection programs in specific occupational environments such as coke ovens and coal conversion facilities.

3. Physiology/Ergonomics:

   a. Studies to assess the long-term effect of breathing increased oxygen and carbon dioxide concentrations under positive pressure, particularly at moderate to high work rates for intervals of time ranging from 20 minutes to 4 hours.

4. Medicine:

   a. Development of medical surveillance guidelines for respirator users.

   b. Development of physical and psychological predictors of user ability to wear respirators.

   c. Studies which quantitatively define the effects of respirator usage on specific medical conditions.

   d. Studies of the relationship of smoking, respirator use, and pulmonary dysfunction.

e. Studies of the effects of sensory deprivation produced by respirator use.

f. Studies involving motivational aspects of respirator use.

g. Studies of the effects of respirator use upon certain physiological functions, such as cardiovascular, pulmonary, lung clearance, and renal.

5. Chemistry:

a. Studies leading to the development of a rapid nondestructive method for determining sorbent efficiencies which could be easily employed for routine quality control by both manufacturers and users.

b. Studies which will identify and characterize the critical sorbent/contaminant interaction factors and thus allow the development of a model for effectively predicting breakthrough times for compounds, classes of compounds, combinations of contaminants, sorbent penetration, sorbent-contaminant reaction products, etc.

c. Studies to develop better absorbents for general classes of contaminants and/or specific substances. Of particular interest would be sorbent materials suitable for highly polar low boiling compounds, ethylene oxide, etc.

6. Aerosol Science:

a. Development of rapid, nondestructive methods for testing filter efficiency, particularly under field conditions.

b. Studies to determine whether or not existing test methods adequately predict the effectiveness of filters in removing fibrous particulates, and if not, develop an effective method.

c. Development of novel, low-resistance, high efficiency particulate filtration methods.

V. REVIEW PROCEDURE AND CRITERIA

A. Applications responsive to this request for applications will be reviewed by an appropriate peer review group on the basis of the following criteria:

1. Training, experience, and research competence, or promise, of the applicant(s) to carry out the proposed investigations, and the adequacy of effort (time) to be devoted to the project.

2. The scientific merit of the proposal: the questions proposed for study, the research design, the proposed methodology, the proposed methods for analysis and interpretation of data.

3. Adequacy and suitability of the existing and proposed facilities and resources.

4. Appropriateness of the requested budget relative to the work proposed.

5. Adequacy of collaborative arrangement(s), if applicable.

B. Demonstration Grant applications will be reviewed additionally on the basis of the following criteria:

1. Degree to which project objectives are clearly established, obtainable, and for which progress toward attainment can and will be measured.

2. Availability, adequacy, and competence of personnel, facilities, and other resources needed to carry out the project.

3. Degree to which the project can be expected to yield or demonstrate results that will be useful and desirable on a national or regional basis.

4. Documentation of expected cooperation of industry, unions, or other participants in the project, where applicable.

C. A secondary review process will be conducted by NIOSH. Factors considered in this review include:

1. The results of the initial review.

2. The significance of the proposed research to the research program of NIOSH.

3. National needs and program balance.

4. Policy and budgetary considerations.

D. Proposals considered to be nonresponsive to the terms outlined in this request will be appropriately reassigned for review or returned to the investigator, as indicated.

VI. APPLICATION AND AWARD

Applications should be submitted on form PHS 398 (Revised 10/79) or PHS 5161-1 for State and local government applicants. Application kits may be obtained from:

Office of Grants Inquiries
Division of Research Grants
National Institutes of Health
Westwood Building - Room 448
Bethesda, Maryland 20205

Telephone: (301) 496-7441

Care should be taken in following the instructions included with the application form, making certain to fulfill the points identified under the heading "REVIEW CRITERIA." Line 2 of the application should be checked "yes" and the title of the Request for Applications should be entered (NIOSH-PROTECTION FROM AIRBORNE TOXIC AND CARCINOGENIC MATERIALS BY RESPIRATORY PROTECTION SYSTEMS).

An original and six copies of the application (original and two copies for State and local governments) must be received no later than November 1, 1982, in order to be considered in the February/March 1983 Study Section review. Applications received after November 1, 1982, will be returned to the originator. Completed applications must be sent or delivered to:

Application Receipt
Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
Bethesda, Maryland 20205

A brief covering letter should accompany the application indicating that it is submitted in response to this Request for Applications. A carbon copy of the covering letter along with an additional copy of the application should be sent to the Acting Chief, Grants Administration and Review Branch (see below).

An applicant organization has the option of having specific salary and fringe benefit amounts for individuals omitted from the copies of the application that are made available to outside reviewing groups. If the applicant organization elects to exercise this option, asterisks should be used on the original and six copies of the application to indicate those individuals for whom salaries and fringe benefits are being requested; the subtotals must still be shown. In addition, submit an additional copy of page four of form PHS-398, completed in full with the asterisks replaced by the amount of the salary and fringe benefits requested for each individual listed. This budget page will be reserved for internal PHS staff use only.

For further information contact:

Jack E. McCracken, Ph.D.
Acting Chief
Grants Administration and Review Branch
National Institute for Occupational
Safety and Health
Parklawn Building - Room 8-63
5600 Fishers Lane
Rockville, Maryland 20857

Telephone: (301) 443-4493 or

Mr. Joseph West
Grants Management Officer
National Institute for Occupational
  Safety and Health
Parklawn Building - Room 8-23
5600 Fishers Lane
Rockville, Maryland 20857

Telephone: (301) 443-3122

ANNOUNCEMENT

EXTRAMURAL ASSOCIATES PROGRAM

NATIONAL INSTITUTES OF HEALTH

Application Receipt Date: December 31, 1982

The National Institutes of Health (NIH) invites nominations for the 1983-84 Extramural Associates Program to promote the entry and participation of ethnic minorities and women in NIH-supported research.

Temporary appointments of employees between Federal executive agencies, state and local governments, institutions of higher education, and Indian tribal governments, can be effected under the Intergovernmental Personnel Act (IPA) of 1970 (Public Law 91-648). In recent years, significant numbers of personnel from academic institutions have used the IPA mechanism to gain thorough knowledge of research concerns of the NIH, the support through which this research is being accomplished, and the policies and procedures which govern the awarding of grants and contracts. Yet institutions which traditionally contribute to the basic preparation of minorities and women for biomedical science are not utilizing this opportunity to an equal extent. While not excluding any individuals or institutions from the available options under the IPA, the NIH Extramural Associates Program was specially established to redress a noticeable imbalance in the current use of an available opportunity.

The NIH will invite two groups of up to seven key science administrators from schools which contribute significantly to the pool of minorities and women in science, to spend five months in residence in the Washington, D.C. area. Salary and related expenses will be reimbursed by the NIH to the limit allowed under the IPA. In addition, a per diem allowance will be provided to cover the normal cost of living while in Washington, D.C.

While in the Program, the Associates will work in rotating assignments with senior staff members at the NIH and other Federal agencies. They will attend seminars, committee meetings, workshops, site visits and will have the opportunity to gain information concerning legislative, budgetary and other Federal health-related programs associated with grant and contract activities.

The NIH expects that such information will primarily benefit the institutions from which the Associates come, in that they will be the lead resource administrators from whom faculty and students can obtain information about health research programs funded by the NIH. In addition, the NIH expects immediate benefits from the special contributions to be made by these experienced administrators while at the NIH.

Nominations of a candidate will be accepted from the president or an equivalent official of an eligible institution. In addition to the general requirements of the IPA, emphasis for selection of Associates will be on the demonstrated contribution of an institution to the advancement of ethnic minorities and women; on its plan to utilize the Associate's newly gained knowledge; and on the qualifications, experience and interest of the nominee.

All Associates will be required to participate in the program for five months beginning on or about August 1, 1983 or February 1, 1984. **Nominations and completed applications are due by December 31, 1982;** selections will be announced by March 31, 1983.

Additional information concerning the program or the application process may be obtained by writing or calling:

Mrs. Jean G. Oliver, Director
Extramural Associates Program
National Institutes of Health
Building 31 - Room 1B59
9000 Rockville Pike
Bethesda, Maryland 20205

Telephone: (301) 496-9728

☆U.S. GOVERNMENT PRINTING OFFICE: 1982-361-144:207

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NIH GUIDE for GRANTS and CONTRACTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Vol. 11, No. 11, October 8, 1982

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HAVE YOU MOVED?

If your present address differs from that shown on the address label, please send your new address to: Grants and Contract Guide Distribution Center, National Institutes of Health, Room B3BN10, Building 31, Bethesda, Maryland 20205, and attach your address label to your letter. Prompt notice of your change of address will prevent your name from being removed from our mailing list.

The GUIDE is published at irregular intervals to announce scientific initiatives and to provide policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in grants and contracts activities administered by the National Institutes of Health.

Two types of supplements are published by the respective awarding units. Those printed on yellow paper concern contracts: solicitations of sources and announcement of availability of requests for proposals. Those printed on blue paper concern invitations for grant applications in well-defined scientific areas to accomplish specific program purposes.

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NIH GUIDE FOR GRANTS AND CONTRACTS
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NOTICE

NEW FORMS FOR RESEARCH GRANT, RCDA, AND INDIVIDUAL NATIONAL RESEARCH SERVICE AWARD (FELLOWSHIP) APPLICATIONS

Grant Application Forms PHS 398 and PHS 2590

The new application forms for Public Health Service grant (PHS 398, revised May 1982) and for continuation of such a grant (PHS 2590, revised May 1982) are now available for use by the scientific community. Copies of these forms may be obtained by writing to:

Chief, Office Services Branch
Division of Reserch Grants
National Institutes of Health
Bethesda, Maryland 20205

Individual copies may also be obtained by writing to:

Office of Grants Inquiries
Division of Research Grants
National Institutes of Health
Bethesda, Maryland 20205

While the new forms contain a number of changes, the most significant ones are in the areas of research involving human subjects or vertebrate animals. Therefore, if proposed projects involve human subjects or vertebrate animals, use the new forms for submissions after January 1983. But in those cases where human subjects or animals are not involved, please continue to use the 1980 versions of the PHS 398 and PHS 2590 forms until supplies are exhausted.

Individual NRSA Forms PHS 416-1 and PHS 416-9

The new application forms for an Individual National Research Service Award (PHS 416-1, revised December 1981) and for continuation of such an award (PHS 416-9, revised December 1981) will soon be available. The new forms for competing applications should be used for the February 1, 1983 receipt date. Copies of these forms may be obtained by writing to:

Chief, Office Services Branch
Division of Research Grants
National Institutes of Health
Bethesda, Maryland 20205

Individual copies may also be obtained by writing to the following address:

Office of Grants Inquiries
Division of Research Grants
National Institutes of Health
Bethesda, Maryland 20205

NIH Research Career Development Awards (RCDAs)

NIH Research Career Development Awardees (K04) will start using the PHS 2590 continuation application form in the near future. Coincident with this change, the institution control offices will be asked to distribute the application forms. By approximately December 1, 1982, mailings to control offices will include a computerized face page and a set of supplemental instructions for RCDA (K04) continuation applications. The May 1982 revision of the PHS 2590 form will have to be used. Questions on this conversion should be directed to:

Mr. Nicholas Moriarty
Division of Research Grants
National Institutes of Health
Bethesda, Maryland 20205

Telephone: (301) 496-7221

Applicants for new (competing) RCDAs should continue to use the current additional instructions booklet.

ANNOUNCEMENT

BIOMEDICAL RESEARCH SUPPORT GRANT APPLICATIONS

FOR FISCAL YEAR 1983

DIVISION OF RESEARCH RESOURCES

Application Receipt Date: January 1, 1983

I. BACKGROUND

The Biomedical Research Support Grant (BRSG) Program is specifically designed to provide funds on a continuing basis to eligible institutions heavily engaged in health-related research to strengthen their programs by allowing flexibility available to the institutions to meet emerging opportunities in research; to explore new and unorthodox ideas; and to use these research funds in ways and purposes which they (the institutions), in their judgment, feel would contribute effectively to the furtherance of their research program.

II. ELIGIBILITY

Awards are made to non-profit institutions, not directly to individual investigators. Health professional schools, other academic institutions, hospitals, state and municipal health agencies, and research organizations may apply if the institution received a minimum of three allowable PHS biomedical or health-related behavioral research grants, totaling $500,000 (including direct and indirect costs), awarded during FY 1982 (October 1, 1981 through September 30, 1982). Federal institutions and institutions located in a foreign country are not eligible.

NOTE: Other academic includes, as a single eligible component, all other schools, departments, colleges and free-standing institutes of the institution except the health professional schools.

III. AWARD CONDITIONS

The BRSG award is for one year and must be renewed annually. The start date is April 1. It is estimated that approximately 420 BRSG awards will be made in FY 1983.

The BRSG program is described in the catalog of Federal Domestic Assistance, No. 13.337, Biomedical Research Support. Grants will be awarded under the authority of the Public Health Service Act, Section 301 (a) (3); Public Law 86-798, (42 USC 241) and administered under PHS grant policies and Federal Regulations 45 CFR Part 74 and the Biomedical Research Support Grant Information Statement and Administrative Guidelines. This program is not subject to A-95 Clearinghouse of Health Systems Agency review.

The amount of each BRSG award is based upon a formula that is applied to the total of direct and indirect costs awarded for allowable PHS research grants.

IV. METHOD OF APPLYING

BRSG application kits (Form NIH-147-1) will be mailed on or about November 26 to institutions that, according to NIH records, are eligible to apply for a BRSG.

Completed BRSG applications must be received by January 1, 1983.

If an institution believes that it is eligible and has not received an application kit by December 6, call Mrs. Gilda Polletto, Grants Management Specialist, Area Code: (301) 496-5131.

ANNOUNCEMENT

SMALL GRANTS PROGRAM FOR PILOT PROJECTS

BIOTECHNOLOGY RESOURCES PROGRAM

DIVISION OF RESEARCH RESOURCES

Application Receipt Dates: February 1, June 1, October 1

The Biotechnology Resources Program (BRP) of the Division of Research Resources (DRR) has initiated a small grant award beginning with the February 1 application receipt date in 1983. The BRP expects to make approximately ten to twenty awards for Fiscal Year 1983, contingent on receipt of meritorious applications and appropriated funds.

I. PURPOSE OF THE AWARD

This is a one-year, non-renewable award for pilot projects in high technology and engineering related to biomedical research. The projects should involve feasibility studies of innovative and high-risk ideas and provide a basis for more extended research in the project's technology.

The purpose of the Biotechnology Resources small grants program is to:

1. Enable examination of a new technology for its usefulness in biomedical research; or
2. Develop significant changes in existing technology important to biomedical research; or
3. Translate scientific notions into a basis for a future technology.

II. ELIGIBLE APPLICANTS

This program is open to both non-profit and for-profit organizations and is designed to support:

1. Engineers and other scientists with experience primarily in fields other than biomedical research. (The BRP has a New Investigator Research Award program for recently trained or less experienced scientists.)

This program is described in the Catalog of Federal Domestic Assistance No. 13.371, Biotechnology Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 42 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

2. Investigators whose research career in high technology has been interrupted and is to be resumed.

3. Investigators changing field of research.

4. Investigators at minority institutions or located in a largely non-research environment such as a small business.

5. Established investigators needing quick support for a high technology proposal for which no other funds are available.

The award may not be used to supplement support for an ongoing project.

III. APPLICATION AND REVIEW PROCEDURE

Applications shall be submitted on Form PHS 398, available at most institutional business offices or from the Division of Research Grants, NIH. Because the format for preparing this application is different from that used for regular research grants, additional information and instructions should be obtained from BRP staff contact listed below. Applications must adhere to this format to be responsive. Unresponsive applications will be returned to the applicant without review. An accelerated review will be scheduled as follows:

Receipt Date Annually	Institute Committee Review	Council Review	Earliest Date for Funding
February 1	March - April	May-June	June
June 1	July - September	Sept-Oct	November
October 1	November - January	Jan - Feb	February

Applications recommended for approval will either be funded or withdrawn immediately after review by the National Advisory Research Resources Council.

IV. REVIEW CRITERIA

Applications will be evaluated with respect to the following criteria: The significance and scientific merit of the proposed project; its characterization as an innovative and high-risk pilot project in high technology or engineering which is relevant to biomedical research and will provide a basis for more extended research; the methodology, including choice of experimental methods, equipment or materials; the investigator's background and training for carrying out the project; adequacy of the available and requested facilities; and the adequacy of justifications presented for budget requests.

V. FUNDING CRITERIA

Applications will compete with each other in accordance with scientific merit and the purposes of the small grant program.

VI. TERMS OF THE AWARD

The award will provide a maximum of $15,000 (direct costs) for personnel consultants, supplies, small equipment, and travel required by the project.

VII. STAFF CONTACT

For further information prospective applicant are strongly urged to contact:

Dr. William R. Baker, Jr.
Special Assistant for Biomedical Engineering
Biotechnology Resources Program
Division of Research Resources
National Institutes of Health
Building 31 - Room 5B43
9000 Rockville Pike
Bethesda, Maryland 20205

Telephone: (301) 496-5411

ANNOUNCEMENT

GENETIC SEQUENCE DATA BANK

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

The National Institute of General Medical Sciences (NIGMS) announces the international availability of a new public resource, the Genetic Sequence Data Bank (GenBank). GenBank is a repository of all published nucleic acid sequences greater than fifty nucleotides in length, annotated and checked for accuracy. This resource, co-sponsored by the NIGMS, National Cancer Institute, National Institute of Allergy & Infectious Diseases, Division of Research Resources, Department of Energy, Department of Defense and the National Science Foundation, is of particular interest to geneticists and molecular biologists. Nucleic acid sequences are available from the bank for a modest fee on computer readable magnetic tape and by limited dial-up on-line access. In addition, a yearly hard-copy edition of the data bank will be available.

For information write:

GenBank
c/o Computer Systems Division
Bold Beranek & Newman, Inc.
10 Moulton Street
Cambridge, Massachusetts 02238

ANNOUNCEMENT

RESEARCH GRANTS ON SMALL ANIMAL MODELS FOR SCREENING ANTIEPILEPTIC DRUGS

NATIONAL INSTITUTE OF NEUROLOGICAL AND COMMUNICATIVE DISORDERS AND STROKE

Application Receipt Dates: March 1, July 1, November 1

I. INTRODUCTION

The Epilepsy Branch, Neurological Disorders Program of the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS), encourages the submission of research grant applications (R01) for the development of small animal models to be used in the screening of antiepileptic drugs.

II. BACKGROUND

Even though more than 2 million Americans currently suffer from epilepsy, the development of effective yet nontoxic antiepileptic drugs has proceeded slowly. In 1977, the Commission for the Control of Epilepsy and its Consequences recommended continued Federal funding for new drug development and advised the expansion of animal screening for potential antiepileptic drugs. To keep pace with the development of new concepts in epileptogenesis, there needs to be a concerted long-range effort by the scientific community to provide new, easily used models of modest cost for screening potential anticonvulsants. Current seizure models evaluate drug effects on the spread of seizures induced by maximum electroshock (MES) and on seizure threshold when the threshold is lowered by subcutaneous pentylenetetrazol. These tests have not changed substantially since their development nearly 50 years ago. Despite the fact that they are inexpensive, easy to do, and can be standardized, there is increasing uncertainty about the relationships between the models and modern concepts of epileptogenesis. The current models therefore may potentially impede progress by not detecting a promising useful drug. False negatives may cause a whole class of compounds to be set aside and never identified as having therapeutic potential. The Epilepsy

---

This program is described in the Catalog of Federal Domestic Assistance No. 13.854, Fundamental Neurosciences. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

Branch, neurological Disorders Program, NINCDS, encourages the submission of applications for the support of basic research on development of new animal models specifically for the screening of antiepileptic drugs.

III. RESEARCH GOALS

It is recognized that good animal models expedite research by permitting drugs to be tested with the confidence that results can be extrapolated accurately to humans. The ideal model for testing the effects of antiepileptic drugs would be one that closely approximates human epilepsy, is simple and inexpensive, and from which results could be obtained easily and quickly. Several existing methods of inducing seizures may be potentially useful for the development of models of epilepsy for evaluation of anticonvulsant drugs. Research grant applications should focus on validation of the relationship of seizure models to human epilepsy and demonstration that the animal models are accurate, reproducible, and sensitive to a variety of drugs and compounds. The primary research goal therefore is the development of models which 1) lend themselves to rapid and inexpensive screening of new antiepileptic drugs; 2) have a validity for seizures in man; 3) are superior to the standard assays already in use; and 4) are capable of predicting anticonvulsant activity for one or more of the specific types of seizures in man. To validate the model, it must be demonstrated that 1) electrographic studies show the presence of epileptic-like activity in the EEG, and 2) clinical seizure activity is observable.

IV. MECHANISMS OF SUPPORT

Support for this program will be through the regular research project grant-in-aid. Each successful applicant will plan, direct, and carry out the individual research project.

V. APPLICATION AND REVIEW PROCEDURES

Applications should be prepared on form PHS 398 (Revised 5/80) following instructions contained in the application kit. Application kits are available from most institutional business offices, or may be obtained from the Division of Research Grants, at the address given below.

Applications must be responsive to the program announcement and the goals of NINCDS. They will be judged on scientific merit and program relevance in accordance with NIH policy and procedures involving peer review. An initial review will be made by an appropriate study section of the Division of Research Grants. A second level of review will be made by the National Advisory Neurological and Communicative Disorders and Stroke Council.

Deadline dates for the receipt of applications are March 1, July 1, and November 1 annually.

The phrase "NINCDS Program Announcement for Small Animal Models for Screening Antiepileptic Drugs" should be typed in space No. 2 of the face page of the application. The original and six copies of the application should be mailed to:

Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205

One copy of the application is to be sent to the addressee below. Also, for further information applicants may contact:

William H. Pitlick, M.D.
Health Scientist Administrator
Epilepsy Branch
Neurological Disorders Program
National Institute of Neurological and
Communicative Disorders and Stroke
Federal Building - Room 118
7550 Wisconsin Avenue
Bethesda, Maryland 20205

Telephone: (301) 496-1917

ANNOUNCEMENT

USE OF GROWTH FACTORS, MATURATION FACTORS AND ANTI-GROWTH FACTORS IN ANIMAL TUMOR MODELS

BIOLOGICAL RESPONSE MODIFIERS RESEARCH

NATIONAL CANCER INSTITUTE

Application Receipt Dates: March 1, July 1, November 1

The National Cancer Institute's (NCI) Division of Cancer Treatment (DCT) desires to expand its support of clinical treatment research. The program is seeking applications for research grants concerned with the therapeutic effects of growth factors, maturation factors, and monoclonal antibody to growth factors on the growth and metastasis of cancer in animal tumor models. In making this program announcement it is not the intent of the NCI to make or imply any delimitation related to biological response modifiers research, but rather to stimulate investigator initiated research in biological response modifiers.

Applications in response to this announcement will be reviewed in accordance with the usual National Institutes of Health (NIH) peer review procedures. They will first be reviewed for scientific and technical merit by a review group composed mostly of non-Federal scientific consultants. Following this initial review, the application will be evaluated for program relevance by the National Cancer Advisory Board. The review criteria customarily employed by the NIH for regular research grant applications will prevail.

DEADLINE

Applications will be accepted in accordance with the usual NIH receipt dates for new applications. Deadline dates are: March 1, July 1, November 1.

METHOD OF APPLYING

Applications should be submitted on form PHS 398, which is available in the grants and contracts business office at most academic and research institutions or from the Division of Research Grants (DRG), NIH. In space #2 on the first page of this form, indicate the title of the Program Announcement.

This program is described in the catalog of Federal Domestic Assistance No. 13.395, Cancer Treatment Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

Additionally, a brief covering letter should accompany the application indicating it is being submitted in response to this program announcement. The original and six copies of the application should be sent or delivered to:

Application Receipt Office
Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
Bethesda, Maryland 20205

For further information, investigators are encouraged to contact:

Dr. Cedric W. Long
Program Director for Pre-Clinical
Trials, BRB, BRMP
Building 426 - Room 1
Frederick Cancer Research Facility
Frederick, Maryland 21701

Telephone: (301) 695-1098

In order to alert the DCT to the submission of proposals with primary thrust directed to biological response modifiers research, a copy of the covering letter should be sent under separate cover to Dr. Long.

ANNOUNCEMENT

DEVELOPMENT OF GENETICALLY ENGINEERED CELL PRODUCTS

BIOLOGICAL RESPONSE MODIFIERS RESEARCH

NATIONAL CANCER INSTITUTE

Application Receipt Dates: March 1, July 1, November 1

The National Cancer Institute's (NCI) Division of Cancer Treatment (DCT) desires to expand its support of clinical treatment research. The program is seeking applications for research grants concerned with the development of genetically engineered cell products for therapeutic application as biological response modifiers. This announcement will support diverse approaches into the use of genetic engineering to transpose genes coding for biological response modifiers such as interferons, lymphokines, growth factors and other gene products into microbial organisms for a large scale production, isolation, purification and characterization of these factors for therapeutic application as biological response modifiers. In making this program announcement it is not the intent of the NCI to make or imply any delimitation related to biological response modifiers research, but rather to stimulate investigator initiated research in biological response modifiers.

Applications in response to this announcement will be reviewed in accordance with the usual National Institutes of Health (NIH) peer review procedures. They will first be reviewed for scientific and technical merit by a review group composed mostly of non-Federal scientific consultants. Following this initial review, the application will be evaluated for program relevance by the National Cancer Advisory Board. The review criteria customarily employed by the NIH for regular research grant applications will prevail.

DEADLINE

Applications will be accepted in accordance with the usual NIH receipt dates for new applications. Deadline dates are: March 1, July 1, November 1.

METHOD OF APPLYING

Applications should be submitted on form PHS 398, which is available in the grants and contracts business office at most academic and research institutions or from the Division of Research Grants (DRG) NIH. In space #2 on the first page of this form, indicate the title of the program announcement.

This program is described in the catalog of Federal Domestic Assistance No. 13.395, Cancer Treatment Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

Additionally, a brief covering letter should accompany the application indicating it is being submitted in response to this program announcement. The original and six copies of the application should be sent or delivered to:

Application Receipt Office
Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
Bethesda, Maryland 20205

For further information, investigators are encouraged to contact:

Dr. Cedric W. Long
Program Director for Pre-Clinical
Trials, BRB, BRMP
Building 426 - Room 1
Frederick Cancer Research Facility
Frederick, Maryland 21701

Telephone (301) 695-1098

In order to alert the DCT to the submission of proposals with primary thrust directed to biological response modifiers research, a copy of the covering letter should be sent under separate cover to Dr. Long.

ANNOUNCEMENT

USE OF TUMOR ASSOCIATED ANTIGENS AS IMMUNOGENS

BIOLOGICAL RESPONSE MODIFIERS RESEARCH

NATIONAL CANCER INSTITUTE

Application Receipt Dates: March 1, July 1, November 1

The National Cancer Institute's (NCI), Division of Cancer Treatment (DCT), desires to expand its support of clinical treatment research. The program is seeking applications for research grants concerned with the development of methods of immunization that evoke effective *in vivo* anti-tumor immunity using purified tumor associated antigens as immunogens. Isolation of tumor associated antigens is now possible using monoclonal antibodies. There is considerable uncertainty, however, how best to administer purified antigens *in vivo* to evoke effective anti-tumor immunity. Certain antigens may facilitate and others may inhibit tumor growth and metastases. The proposed studies should investigate this issue in both normal and tumor bearing animals using purified antigens as therapeutic agents. Preference will be given to non-viral tumor associated antigens on recently derived spontaneous or chemically induced fully syngeneic tumors although consideration will be given to viral coded tumor antigens and even normal cell surface alloantigens as model antigens. The use of various immunization schedules and adjuvants in therapy models with detailed monitoring of the host cellular and immune responses will be required. These studies must be directed toward optimizing the therapeutic effects of these antigens *in vivo* as demonstrated by protection studies against subsequent tumor growth. Proposals to investigate monoclonal antibody purified tumor associated antigens as therapeutic reagents in man may also be submitted. As in the animal models, homogenous preparations of high purity are preferred for these investigations. End points may be assessed by *in vitro* assays or by *in vivo* therapeutic effects. In making this program announcement it is not the intent of the National Cancer Institute to make or imply any delimitation related to biological response modifiers research, but rather to stimulate investigator initiated research in biological response modifiers.

Applications in response to this announcement will be reviewed in accordance with the usual National Institutes of Health (NIH) peer review procedures. They will first be reviewed for scientific and technical merit by a review group composed mostly of non-Federal scientific consultants. Following this initial review, the application will be

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This program is described in the catalog of Federal Domestic Assistance No. 13.395, Cancer Treatment Research. Awards will be made under the authority of the Public Health Service Act, Title III, Secion 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

evaluated for program relevance by the National Cancer Advisory Board. The review criteria customarily employed by the NIH for regular research grant applications will prevail.

DEADLINE

Applications will be accepted in accordance with the usual NIH receipt dates for new applications. Deadline dates are March 1, July 1, November 1.

METHOD OF APPLYING

Applications should be submitted on form PHS 398, which is available in the grants and contracts business office at most academic and research institutions or from the Division of Research Grants (DRG), NIH. In space #2 on the first page of this form, indicate the title of the program announcement.

Additionally, a brief covering letter should accompany the application indicating it is being submitted in response to this program announcement. The original and six copies of the application should be sent or delivered to:

Application Receipt Office
Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
Bethesda, Maryland 20205

For further information, investigators are encouraged to contact:

Dr. Cedric W. Long
Program Director for Pre-Clinical
Trials, BRB, BRMP
Building 426 - Room 1
Frederick Cancer Research Facility
Frederick, Maryland 21701

Telephone: (301) 695-1098

In order to alert the DCT to the submission of proposals with primary thrust directed to biological response modifiers research, a copy of the covering letter should be sent under separate cover to Dr. Long.

ANNOUNCEMENT

DEVELOPMENT OF CELL LINES PRODUCING LYMPHOKINES AND CYTOKINES

BIOLOGICAL RESPONSE MODIFIERS RESEARCH

NATIONAL CANCER INSTITUTE

Application Receipt Dates: March 1, July 1, November 1

The National Cancer Institute's (NCI), Division of Cancer Treatment (DCT), desires to expand its support of clinical treatment research. The program is seeking applications for research grants concerned with the development of cell lines producing lymphokines and cytokines with therapeutic effects as biological response modifiers. This announcement will encourage research in the development of such cell lines and the development of methods to isolate, purify and characterize the therapeutic potential of the various products of these cell lines in appropriate test systems. These products may have a potential longterm usefulness in the treatment of cancer and/or in the alteration of biological responses in the course of cancer. In making this program announcement it is not the intent of the NCI to make or imply any delimitation related to biological response modifiers research, but rather to stimulate investigator initiated research in biological response modifiers.

Applications in response to this announcement will be reviewed in accord with the usual NIH peer review procedures. They will first be reviewed for scientific and technical merit by a review group composed mostly of non-Federal scientific consultants. Following this initial review, the application will be evaluated for program relevance by the National Cancer Advisory Board. The review criteria customarily employed by the NIH for regular research grant applications will prevail.

DEADLINE

Applications will be accepted in accordance with the usual NIH receipt dates for new applications. Deadline dates are March 1, July 1, November 1.

This program is described in the catalog of Federal Domestic Assistance No. 13.395, Cancer Treatment Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

METHOD OF APPLYING

Applications should be submitted on form PHS 398, which is available in the grants and contracts business office at most academic and research institutions or from the Division of Research Grants (DRG), NIH.

In space #2 on the first page of this form, indicate the title of the program announcement.
Additionally, a brief covering letter should accompany the application indicating it is being submitted in response to this program announcement. The original and six copies of the application should be sent or delivered to:

Application Receipt Office
Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
Bethesda, Maryland 20205

For further information, investigators are encouraged to contact:

Dr. Cedric W. Long
Program Director for Pre-Clinical
Trials, BRB, BRMP
Building 426 - Room 1
Frederick Cancer Research Facility
Frederick, Maryland 21701

Telephone: (301) 695-1098

In order to alert the DCT to the submission of proposals with primary thrust directed to biological response modifiers research, a copy of the covering letter should be sent under separate cover to Dr. Long.

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NIH GUIDE for GRANTS and CONTRACTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Vol. 11, No. 12, November 5, 1982

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HAVE YOU MOVED?

If your present address differs from that shown on the address label, please send your new address to: Grants and Contract Guide Distribution Center, National Institutes of Health, Room B3BN10, Building 31, Bethesda, Maryland 20205, and attach your address label to your letter. Prompt notice of your change of address will prevent your name from being removed from our mailing list.

The GUIDE *is published at irregular intervals to announce scientific initiatives and to provide policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in grants and contracts activities administered by the National Institutes of Health.*

Two types of supplements are published by the respective awarding units. Those printed on yellow paper concern contracts: solicitations of sources and announcement of availability of requests for proposals. Those printed on blue paper concern invitations for grant applications in well-defined scientific areas to accomplish specific program purposes.

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NOTICE

SMALL GRANTS PROGRAM

The Division of Research Resources (DRR), National Eye Institute (NEI), National Institute on Aging (NIA), and the National Institute of Dental Research (NIDR) each has previously announced the availability of a small grant award. One of the most attractive features of these one-time awards of up to $15,000 is an accelerated cycle of receipt, review and award of four to five months. Some problems of special handling have arisen which could jeopardize this shortened cycle unless remedied.

NIH urges perspective small grant applicants to give careful attention to the following requirements or suggestions:

-- Obtain special information and instructions for preparation of the application from the appropriate Division or Institute.

-- Clearly identify the mailing envelope as containing a SMALL GRANT APPLICATION.

-- Do not package with other types of applications.

-- Submit the application to Division of Research Grants (DRG) (copies to the Institute) as early as possible, and in all cases in time to arrive at NIH by the published receipt dates of February 1, June 1, and October 1.

Adherence to the above should facilitate prompt processing of the applications within the accelerated period.

REMINDER NOTICE

DEADLINE FOR SUBMISSION OF ASSURANCES OF COMPLIANCE WITH REVISED HUMAN SUBJECTS PROTECTION REGULATIONS

On January 26, 1981, the Department of Health and Human Services (DHHS) published final regulations amending basic DHHS policy for the protection of human research subjects. Institutions holding an Assurance of Compliance were encouraged to implement new provisions of the regulations prior to the negotiation of a revised Assurance of Compliance. Since August, 1981, the Office for Protection from Research Risks (OPRR) has been negotiating Assurances of Compliance with the new regulations.

This notification establishes a deadline of December 31, 1982, for submission of a general (Multiple Project) assurance prepared in accord with DHHS regulations published in the Federal Register on January 16, 1981 (46 FR 8366).

Institutions are encouraged to submit an Assurance of Compliance at the earliest possible date. A sample assurance is available from OPRR (301 - 496-7041). Although it is possible that approval of a multiple project assurance might not be transmitted until sometime after December 31, 1982, institutions may continue to function under their former assurance until such time as approval for the revised assurance is given. Special (Single Project) assurances will continue to be approved on a single project basis. GENERAL ASSURANCES WHICH HAVE NOT BEEN REVISED TO MEET THE 1981 REQUIREMENTS AND SUBMITTED TO OPRR WILL BE TERMINATED EFFECTIVE JANUARY 1, 1983.

NOTICE

EFFECT ON GRANT RECIPIENTS OF PROMPT PAYMENT ACT (P.L. 97-177)

The Prompt Payment Act (P.L. 97-177), which was signed by the President on May 21, 1982, requires Federal agencies to pay their bills on time, to pay interest penalties when payments are made late, and to take discounts only when payments are made within the discount period. Interest penalties will apply to payments made under contracts issued on or after October 1, 1982.

Regarding grant recipients, Section 10 of the final issuance of OMB Circular A-125, "Prompt Payment" (published in the Federal Register, Vol. 47, No. 165, Wednesday, August 25, 1982), states:

> "Grant Recipients. Recipients of Federal assistance may pay interest penalties if so specified in their contracts with business concerns. However, obligations to pay such interest penalties will not be obligations of the United States. Federal funds may not be used for this purpose, nor may interest penalties be used to meet matching requirements of federally-assisted programs."

ANNOUNCEMENT

BIOMEDICAL RESEARCH SUPPORT SHARED INSTRUMENTATION GRANTS

DIVISION OF RESEARCH RESOURCES

Application Receipt Date: February 15, 1982

I. BACKGROUND

As part of its mission to create, develop, and maintain research resources needed by NIH-supported biomedical investigators throughout the nation, the Division of Research Resources (DRR) is continuing its competitive biomedical shared instrumentation grant program initiated in Fiscal Year 1982. The program was established in recognition of the long-standing need in the biomedical research community to cope with rapid technological advances in instrumentation and the rapid rate of obsolescence of existing equipment. The objective of the program is to make available, to institutions with a high concentration of NIH extramural research awards, research instruments which can only be justified on a shared use basis and for which meritorious research projects are described.

Eligible institutions may submit more than one application for different instrumentation in the Fiscal Year 1984 review cycle.

II. RESEARCH GOALS AND SCOPE

This program is designed to meet the special problem of acquisition and updating of expensive shared-use instruments which are not generally available through other NIH mechanisms, such as the regular research, program project and center grant programs, the Biomedical Research Support (BRS) Grant Program and other DRR programs such as Animal Resources and the Biotechnology Resources Program. The latter program emphasizes development of the instrument and associated research methodology, research aspects which are not required in the new BRS Shared Instrumentation Program. The BRS Shared Instrumentation Program is intended for a broad community of the NIH supported investigators.

This program is described in the Catalog of Federal Domestic Assistance No. 13.337, Biomedical Research Support. Awards will be made under the authority of the Public Health Service Act, Secion 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 42 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

III. ELIGIBILITY

The shared instrumentation grant program is a subprogram of the BRS Grant Program of DRR. Awards are made under the authority of the authority of the BRS program and are made to institutions only, not to individuals. In FY 1984, eligibility is limited to those grantees which received a BRS grant award in FY 1983. NIH records will be used to verify eligibility. Applications will be received only once per year. The program is highly competitive. It is expected that a minimum of 25 and a maximum of 75 awards would be made in 1984, depending on the availability of FY 1984 funds.

IV. MECHANISM OF SUPPORT

BRS Shared Instrumentation Grants provide support for expensive state-of-the-art instruments utilized in biomedical research. Aplications are limited to instruments that cost at least $100,000 per instrument or system. Types of instrumentation supported include, but are not limited to, nuclear magnetic resonance systems, electron microscopes, mass spectrometers, protein sequencer/amino acid analyzers and cell sorters. Support will not be provided for general purpose equipment or "stand alone" computer systems.

Awards will be made for the direct costs of acquisition of new, or the updating of existing, research instruments. The institution must meet those costs (not covered in the normal purchase price) required to place the instrumentation in operational order as well as the maintenance, support personnel and service costs associated with maximum utilization of the instrument. There is no upper limit on the cost of the instrument, but the maximum award is $300,000. Grants will be awarded for a period of one year and are not renewable. Supplemental applications will not be accepted. The program does not provide indirect costs or support for construction or alterations and renovations. If the amount of funds requested does not cover the total cost of the instrument, an award will not be made unless the remainder of the funding is assured. Description of the proposed co-funding must be presented with the application. Assurance of co-funding, signed by an appropriate institutional official, must be presented to DRR prior to the issuance of an award. The shared instrument will not be transferable outside of the institution to which it is awarded.

A major user group of three or more investigators should be identified. Each major user must have NIH peer-reviewed research support at the time of the award. The application must show a clear need for the instrumentation by projects supported by multiple NIH research awards and demonstrate that these projects will require at least 75% of the total usage of the instrument. Major users can be individual researchers, or a group of investigators within the same department or from several departments at the applicant institution. NIH extramural awardees from other institutions may also be included.

If the major user group does not require total usage of the instrument, access to the instrument can be made available to other users upon the advice of the advisory committee. These users need not be NIH awardees but priority should be given to NIH supported scientists engaged in biomedical research.

A progress report shall be required for each of the three years following receipt of the award. The report must describe the use of the instrument, listing all users, and indicate the value of the instrumentation to the research of the major users and to the institution as a whole.

V. ADMINISTRATIVE ARRANGEMENTS

Each applicant institution must propose a Principal Investigator who can assume administrative/scientific oversight responsibility for the instrumentation requested. An internal advisory committee to assist in this responsibility should also be utilized. It is expected that in most cases, the BRS Program Director and extant BRS advisory apparatus, augmented with members having technical and scientific expertise regarding the instrumentation requested, can serve this function. However,there may be circumstances where other existing or proposed arrangements are more appropriate for the applicant institution.

In any event, the Principal Investigator and the advisory group are responsible for the development of guidelines for shared use of the instrument, for preparation of all reports required by the NIH, for relocation of the instrument within the grantee institution if the major user group is significantly altered and for continued support for the maximum utilization and maintenance of the instrument in the post award period.

A plan should be proposed for the day-to-day management of the instrument including designation of a qualified individual to supervise the operation of the instrument and to provide technical expertise to the users. Specific plans for sharing arrangements and for monitoring the use of the instrument should be described.

VI. REVIEW PROCEDURES AND CRITERIA

Applications are reviewed by specially convened initial review groups by the Division of Research Grants (DRG) for scientific and technical merit and by the BRS Subcommittee of the General Research Support Review Committee and the National Advisory Research Resources Council of the DRR for program considerations. Funding decisions are the responsibility of the DRR and will not be made prior to November 1, 1983.

Criteria for review of applications include the following:

1. The extent to which an award for the specific instrument would meet the scientific needs and enhance the planned research endeavors of the major users by providing an instrument that is unavailable or to which availability is highly limited.

2. The availability and commitment of the appropriate technical expertise within the major user group or the institution for use of the instrumentation.

3. The adequacy of the origanizational plan and the internal advisory committee for administration of the grant including sharing arrangements for use of the instrument.

4. The institution's commitment for continued support of the utilization and maintenance of the instrument.

5. The benefit of the proposed instrument to the overall research community it will serve.

VII. METHOD OF APPLYING

A. Application Format

Applications are to be submitted on the standard PHS research grant application form (PHS-398, Rev. 5/80) available from most institutional business offices or the Division of Research Grants, National Institutes of Health. Instructions supplied with these forms should be followed except for the following:

1. Face page of the application -

   a. Item 1. The instrument requested should be named in the title of the proposal.

   b. Item 2. Write in "DRR-BRS SHARED INSTRUMENTATION GRANT."

   c. Item 6. Write in January 1, 1984 - December 31, 1984.

   d. Item 12. Complete Item 12 and type in the institution's BRS grant number.

   (Note at the bottom of the page if a duplicate application has been sent to another agency.)

2. Application page 2. Identify the Principal Investigator, the major user group and the complete grant number(s) for each of the users currently active NIH research support.

3. Application page 4. A detailed breakdown of the direct costs requested will be shown on the budget page. Provide a complete description of the instrument including manufacturer, model number and cost including tax and import duties, if applicable. If possible, the model chosen should be justified by comparing its performance with other available instrumenmts.

4. Application page 5. Budget Estimates for All Years. Not applicable; do not submit.

5. Biographical Sketch. In addition to the personnel listed on page 2, include a biographical sketch of the person(s) who will be in charge of maintenance and operation of the instrument and a brief statement of the qualifications of the individual. Biographical sketches should not exceed 2 pages for each individual.

6. Section 2 of the application. Provide information relative to the points identified under criteria for review including:

   a. A description of similar instruments existing at the institution or at nearby institutions and a justification why new or updated equipment is needed. A clear justification should be given for the choice of the instrument and ancillary accessories requested.

b. A description, by major users, of the research projects for which the instrumentation is required. The descriptions need not be of the detail of a regular research grant application (should not exceed 4 pages per major user) but should point out the benefit of the proposed instrument to the research objectives of each major user. An estimate of the percentage use of each project should be given. If there are more than four major users, set up a table listing the names of the users, the NIH grant number, the estimated percentage use and the title of each research project.

c. A description of the organizational plan including the internal advisory committee for administration of the grant.

d. A specific plan and a statement of institutional commitment to operate and maintain the instrument for its useful life at the same utilization level after termination of the three-year reporting period to DRR.

B. Application Procedure

Applications must be received by February 15, 1983. Applications received after this date will not be accepted for review in this competition. The original and six copies should be sent to:

Application Receipt Office
Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
533 Westbard Avenue
Betheda, Maryland 20205

Iniquiries and three copies of the application should be addressed to

Biomedical Research Support Grant Program
Division of Research Resources
Building 31 - Room 5B23
National Institutes of Health
Bethesda, Maryland 20205

Information about eligibility for FY 1983 awards can be obtained by calling Mrs. Gilda Polletto (301) 496-5131)

ANNOUNCEMENT

THE NIEHS CLINICAL INVESTIGATOR AWARD

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

Application Receipt Dates: February 1, June 1, October 1

I. SUMMARY AND PURPOSE

The National Institute of Environmental Health Sciences announces the availability of NIEHS Clinical Investigator Awards for the purpose of developing clinical investigators in the field of environmental health/human toxicology. The award is made to support the research development of clinicians to work with research teams on problems arising from the exposures of human populations to environmental chemicals. (It is not meant to support the activities of "poison centers" and related researchers who deal with the effects of acute exposures to self-inflicted or accidentally inflicted toxic materials or clinical research on the toxicities of pharmaceuticals and other drugs).

The award is designed to further the growth of superior candidates toward independent clinical research in this field and to assist in the development of clinical research programs in environmental health. It will enable successful candidates to investigate for a period not to exceed three years, a well-defined problem under the guidance of an active clinical researcher who has the knowledge, experience, and background required to be a mentor in this field. Usually this experience will take place at another institution or department. An additional two years of support is provided at the end of the research to allow the awardee to return to his/her home institution to develop a program in clinical research in this field. The institution providing for the early research development phase should be able to provide laboratory experience in experimental toxicology as well as the opportunity to study the clinical effects of human exposures to environmental agents. The preceptor should be a clinical investigator experienced in the identification, recognition and assessment of the health effects of such exposures.

The NIEHS Clinical Investigator Award seeks to foster new clinical research departments in the area of environmental toxicology by providing intensive guided research experience for investigators who will establish such departments. There are two acceptable programs; one where the preceptor(s) for the research development of the candidate is at the applicant institution and one in which the preceptor(s) is at another institution. In either case, the applicant institution is responsible for management of the award.

This program is described in the Catalog of Federal Domestic Assistance No. 13.894, Environmental Health Research Manpower Development Resources. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency Review.

II. ELIGIBILITY

A. Candidate:

Applications will be considered on behalf of individuals holding health professional degrees in the clinical sciences (M.D., D.O., or equivalent) who have not previously served as principal investigators on PHS supported research projects (including New Investigator Research Awards). Candidates should have at least two years of clinical training at the postdoctoral level by the projected start of the award. Individuals with experience levels falling outside these limits who believe they may still fulfill the intent of the award are invited to discuss their eligibility with staff and to submit special justification with their application. Candidates should have broad training, should demonstrate individual competence in clinical activities, and should show research potential in the chosen area of interest. Candidates should provide evidence of a serious intent for an academic career related to that area. This grant is intended to provide guided research experience for clinicians in the transition between fellowship or trainee experience and a career in independent investigation. It is not intended for those individuals whose stage of development would make them fully competitive for regular research project awards. Holders of the Ph.D. or comparable research degrees, either with or without an accompanying health professional degree, are not eligible for the Clinical Investigator Award.

A noncitizen is not eligible to apply unless lawfully admitted to the United States for permanent residence.

B. Institutions:

Both the grantee and/or research development institutions must be domestic universities, medical schools, or comparable institutions. The research development institution should have a strong, well-established, research and training program in the chosen area, an adequate number of highly experienced faculty in clinical and basic departments relevant to the chosen area, and interest and capacity to provide guidance to clinically trained individuals in the development of research independence. The grantee institution should include plans for program development commensurate with the training of the candidate.

C. Preceptor:

The candidate's primary preceptor must be a competent investigator in the area of the proposed research activity, who is currently active as an investigator, and who will personally provide the candidate a significant portion of the research supervision he receives. The preceptor may have either a basic science or clinical professional background.

Determination of the acceptability of applications is made by the National Institutes of Health.

III. CONDITIONS OF THE AWARD

The Clinical Investigator Award is made for a total nonrenewable and nontransferable period of five years (three years for research development plus two years for program development as described under Summary and Purpose). Support is based on a full-time, twelve-month staff appointment. The award will provide salary support not to exceed $30,000 annually from NIEHS funds for the five-year period. The actual salary must be consistent with the established salary structure of the grantee institution for persons of equivalent qualifications, experience, and rank. Up to a total of $10,000 annually will be provided for supplies, equipment, travel, etc., which are necessary for pursuit of the Awardee's research program. Funds will be provided for the reimbursement of actual indirect costs at a rate of up to, but not to exceed, eight percent of the total allowable direct costs. When requested, the grantee institution's share of the fringe benefits may be paid as a direct cost (if not treated as an indirect cost) on that proportion of the employee's salary provided by the NIEHS Clinical Investigator Award.

It is expected that the candidate will spend at least 80 percent of his/her time in research during the development period, with the remainder being divided among other activities such as teaching, practice and consultation, administration, receiving research training, and academic studies. The total of all percentages should equal 100. An appropriate sponsor must assume responsibility and provide guidance for the research development in the chosen areas.

Institutions may apply for awards on behalf of named individuals meeting the above criteria. It is not essential for the applicant institution to commit itself in the application to eventual placement of the candidate on its permanent, full-time faculty, but it is expected that institutions will choose candidates who will be able to meet the criteria for making that decision. Evidence of the commitment of the institution to the candidate's research development must be provided.

The Awardee should plan to submit a research project grant application in clinical environmental health sciences prior to the end of the five-year award. Proposals may be submitted at any time so that research support may be available at the completion of the research development experience. No salary support for the investigator may be requested from the research grant application for the time during which the salary support is from the Clinical Investigator Award. Funds to support research, travel, supplies, equipment may be requested.

IV. REVIEW CRITERIA:

Applications for the NIEHS Clinical Investigator Award receive initial merit review by an NIEHS review committee and subsequently by the National Advisory Environmental Health Sciences Council.

Criteria for review include:

- Candidate's development in research and clinical experience in the specified area of interest.
- Candidate's plans for research development.
- Candidate's potential for a career in independent research in the area proposed.

- Candidate's commitment to a research career in the area of interest.
- Technical merit of the research proposal.
- Research development institution's ability to provide the clinical research experience and guidance required to develop the candidate into an independent clinical investigator.
- Ability and plans of the preceptor (or preceptors) who will provide the candidate with the guidance and experience necessary for career development in biomedical research.
- Presence of highly qualified and experienced faculty at the research development institution.
- Applicant institution's commitment to providing the facilities and opportunities necessary to the individual's research development during years four and five.
- Applicant institution's plans for program development in clinical environmental health research upon return of the candidate.

V. APPLICATION AND FURTHER INFORMATION

Applications for NIEHS Clinical Investigator Awards are accepted in accord with the usual NIH application-receipt dates of February 1, June 1, and October 1. It is important that potential applicants consult with staff of the NIEHS prior to the submission of applications to determine if the proposed program fits the criteria and the mission of the Institute. Further information and application materials may be obtained from:

Christopher O. Schonwalder, Ph.D.
Program Director
Research Manpower Development Section
Scientific Programs Branch
Extramural Program

Telephone: (919) 541-7634

ANNOUNCEMENT

NIGMS SHARED INSTRUMENTATION GRANTS

NATIONAL INSTITUTE OF GENERAL MEDICAL SERVICES

Application Receipt Date: February 15

The National Institute of General Medical Sciences (NIGMS) reannounces the availability of a grant mechanism for the acquisition of new, or the updating of existing, major research instruments which cannot be justified fully for use on a single project but which can serve several projects on a shared basis. The intent of this grant is to provide NIGMS grantees with better access to modern instrumentation and to encourage the sharing of expensive equipment. Although the needs of NIGMS grantees are the primary basis on which these shared instrumentation grants will be awarded, access to the instruments provided by this mechanism will not be restricted to NIGMS grantees nor to investigators within the particular grantee institution.

Within any given year, limited funds may be available for this type of grant. Competing demands of regular research grants on the Institute's budget will be a factor in determining the number of awards to be made.

I. MECHANISM OF SUPPORT

Each NIGMS Shared Instrumentation Grant will provide support for an instrument, instrument system, or for the upgrading of an existing system. Each item or system must cost at least $30,000. Stand-alone computers or relatively routine general purpose equipment, such as scintillation counters or preparative ultracentrifuges, will not be considered for an award. Grants will be awarded for a period of up to three years and are not renewable. Besides the cost of the instrumentation, support for maintenance of the equipment may be requested for the period of the grant. In cases where at least 25% of the planned use of the equipment will be by users other than the major user group (see eligibility requirements, below), support for technical assistance up to a maximum of one-half the salary of a qualified technician may be requested for up to three years. Provisions for continued maintenance of the equipment and for technical support beyond the period of the grant must be made by the applicant institution and these plans must be detailed in the application.

Although there is no upper limit to the cost of instrumentation that can be requested, the maximum contribution from NIGMS in the equipment category will

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This program is described in the Catalog of Federal Domestic Assistance Numbers 13.821, Physiology and Biomedical Engineering; 13.859, Pharmacology-Toxicology Research; 13.862, Genetics Research; and 13.863, Cellular and Molecular Basis of Disease Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency Review.

be $200,000 for any one award. If this amount does not cover the total cost of the equipment, an award will not be made unless the remainder of the funding is assured. Assurance of co-funding, signed by an appropriate institution official, must be presented prior to the issuance of an award.

Since the evaluation of an application involves several users and depends so heavily on the particular conditions at a given institution, a grant for shared instrumentation will, in general, not be transferrable between institutions.

II. ELIGIBILITY

The principal investigator on an application for a shared instrumentation grant must hold an active NIGMS research grant and must assume responsibility for the instrument and for all related administrative functions. A major user group of three or more investigators (including the Principal Investigator) must be identified who will use the equipment at least 75% of the time. At least one of this group must have sufficient expertise to instruct others in the use of the equipment and to oversee its appropriate use. Each major user must have NIH research support at the time of award and at least one-half, but a minimum of two, of the major users must hold NIGMS grants. If the major user group does not need the equipment for 100% of the available instrument time, up to 25% of the time may be made available to other users. These other users need not have NIH grant support.

III. APPLICATION PROCEDURES

A. Application Format

Applications are to be submitted on the standard PHS research grant application form (PHS-398, Rev. 5/80) available from most institutional business offices or from the Division of Research Grants, NIH. Instructions supplied with these forms should be followed except as described below:

1. Face page of the application

   a. Item 1. The instrument requested should be named in the title of the proposal.

   b. Item 2. Write in "NIGMS SHARED INSTRUMENT GRANT"

2. Application page 2. Identify the principal investigator and each member of the major user group. Identify, by grant number, the currently active NIH research support for these individuals.

3. Application page 4. A detailed breakdown of the direct costs requested should be shown on the budget page. Provide a complete description of the instrument including manufacturer, model number and cost including tax and import duties, if applicable. If possible, the model chosen should be justified by comparing its performance with other available instruments.

4. Biographical Sketch. In addition to the personnel listed on page 2, include a biographical sketch of the person(s) who will be in charge of maintenance and operation of the instrument and a brief statement of the qualifications of that individual. Biographical sketches should not exceed two pages for each individual.

Section 2 of the application. Provide information relative to the points identified under criteria for review including:

1. A description of similar instruments existing at the institution or at nearby institutions and a justification as to why new or updated equipment is needed. A clear justification should be given for the choice of the instrument and for ancillary accessories requested.

2. A description, by major users, of the research projects for which the instrumentation is required. The descriptions need not be of the detail found in a regular research grant application (should not exceed 4 pages) but should point out the benefit of the proposed instrument to the research objectives of each major user. An estimate of the percentage use of the instrument time for each project should be given. In cases where the instrumentation will be available to users other than the major user group, a plan for providing access to those users should be detailed.

3. A description of the organizational plan for administration of the grant.

4. A specific plan and a statement of institutional commitment to operate and maintain the instrument for its useful life at the same utilization level after termination of the three-year period of NIGMS support. A commitment from the institution for necessary space or renovation will be required.

IV. CRITERIA FOR REVIEW

A. The following factors will be considered in the peer review of shared instrumentation grants.

1. Need for instrumentation. The needs of both the major user group and other potential users will be considered in assessing need.

2. The extent to which an award for the specific instrument would meet the scientific needs and enhance the planned research endeavors of the major users by providing an instrument that is unavailable or to which availability is highly limited.

3. Appropriate expertise within the major user group for use of the instrumentation.

4. Adequacy of arrangements for sharing of the equipment and for making it accessible to users other than the major user group when this is part of the justification for the instrument.

5. Institutional commitment for continued support and maintenance of the equipment - this may be through user charges if adequate grant support can be demonstrated.

V. CRITERIA FOR AWARDS

A. Due to the limitation of funds available to this program, additional criteria may be considered by the Institute in making funding decisions. They may include:

1. Geographic distribution of awards.
2. Balance between types of instruments supported.

VI. RECEIPT AND REVIEW

There will be one receipt date annually - February 15 of each year. Review will be by review groups specially constituted according to the types of applications received. Applications will go to Council in October of the same year and awards will be made no earlier than December 1 of that year.

Inquiries can be addressed to:

Dr. Marvin Cassman
National Institute of General
Medical Sciences
National Institutes of Health
Bethesda, Maryland 20205

Telephone: (301) 496-7463

At the time a formal application is mailed to the Division of Research Grants, the applicant should inform the individual designated above, in writing, that the application has been submitted. The original and six copies of the application should be sent or delivered to:

Application Receipt Office
Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205

ANNOUNCEMENT

RESEARCH ON INFECTIOUS DISEASES IN THE ELDERLY

NATIONAL INSTITUTE ON AGING

NATIONAL INSTITUTE ON ALLERGY AND INFECTIOUS DISEASES

Application Receipt Dates: February 1, June 1, and October 1

The National Institute on Aging (NIA) and the National Institute of Allergy and Infectious Diseases (NIAID) announce a continuing interest in supporting research on infectious diseases in the elderly.

I. BACKGROUND

Morbidity and mortality from infections increase markedly with age. Influenza, pneumonia, and other infections account for a large share of deaths in the elderly. Chronic diseases increase the risk and complications of many infections in older persons. The prevention and treatment of infections in nursing homes and other long-term care settings present problems which have not been systematically studied. Optimal prevention and treatment of infections in the elderly require research on the effects of age-related factors on occurrence and outcomes of infection.

II. RESEARCH GOALS AND SCOPE

A. Epidemiology

1. Prevalence and incidence data are needed regarding many important aspects of infections in the elderly. For infections at several sites (e.g. decubitus ulcers, enteric infections) and by many agents (e.g., respiratory syncytial virus) epidemiologic data are lacking. Altered presentation of tuberculosis and other infections in the elderly may contribute to erroneous prevalence and incidence estimates. Studies of alternative surveillance techniques are needed to clarify this question. Probable differences in patterns of infection between the "young-old" and "old-old" accentuate the need for age-stratified data. Epidemiologic data are needed on nosocomial infections in nursing homes and other long-term care settings.

This program is described in the Catalog of Federal Domestic Assistance Nos. 13.866, Aging Research, and 13.856, Microbiology and Infectious Disease. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

2. Retrospective and prospective studies of infections and their complications in the elderly could clarify their relationship to risk factors such as:

   a. various chronic diseases (e.g., diabetes mellitus and chronic obstructive pulmonary disease);

   b. ambulatory, nutritional, functional, and mental status;

   c. specific types of care settings (acute care hospitals, nursing homes, etc.);

   d. "normal" age-associated changes in the immune system, mucociliary clearance mechanisms, and other functions affecting susceptibility to infection.

B. Pathogenesis and Complications of Infections in the Elderly

The extent, specificity and causes of age-related changes in susceptibility to various human pathogens require further exploration. The relative prevalence of the major pathogenic species and strains in bacterial pneumonia appears to be altered in the elderly. The cause of such changes and the extent to which they are found in other infections remain mostly undertermined. The contribution of age-associated physiologic changes to the reactivation of infections such as tuberculosis and varicella zoster virus also needs examination.

Though age-related changes in some aspects of the immune system (e.g., lymphocyte subpopulations and responses to certain mitogens) have been well-documented in humans, their relationship to the risk of specific infections in the elderly has not been clarified. Additional data are needed on the extent to which possible age-related changes in macrophage and neutrophil function, complement and other "cascade" pathways, chemotactic mechanisms, and the secretory immune system may affect resistance to infections.

There is suggestive evidence that age-related alterations at mucosal surfaces may affect susceptibility to infection. Research is needed on the effects of changes in normal bacterial flora, bacterial adherence, epithelial responses to viral infection (which may in turn affect susceptibility to secondary bacterial infection), and mucociliary clearance mechanisms. The role of other age-associated physiologic changes (such as increased residual bladder volume and increased propensity to aspirate oropharyngeal secretions) needs further study. The effects of deficiencies in phyridoxine and other nutrients on resistance to infection in the elderly also merit consideration.

Complications of many infections appear to be increased in the elderly. Cardiovascular mortality associated with influenza infections appears to be heightened in the elderly. In certain infections, the elderly may be more prone to septicemia and disseminated intravascular coagulation. Research is needed on the potential role of age-associated physiologic changes in predisposing to these and other complications of infections.

For many infections, the effects of "normal" aging on pathogenesis and complications of infections may be less important than the effects of chronic diseases of the elderly and the medical, surgical and diagnostic interventions (e.g., urinary catheterization, prostatectomy, cystoscopy, administration of neurolepticagents) which accompany them. Hence, studies on the pathogenesis of infections in the elderly should address the effects of both aging and chronic disease, and make clear distinctions between them.

C. Diagnosis

Prompt and accurate diagnosis is particularly important in the elderly, who have a reduced rate of recovery from many infections. Despite numerous anecdotal reports of altered presentation of many infections in older persons, there is little objective information on this point, or on the sensitivity and specificity of various diagnostic techniques in the elderly. Reactivity to tuberculin skin tests in the aged shows considerable variability. Increased oropharyngeal colonization in elderly persons with potential bacterial pathogens aggravates problems in the use of sputum cultures in diagnosing pneumonia. Comparisons of the sensitivity and specificity of alternative strategies are needed to increase accuracy and efficiency in diagnosing these and other infections in the elderly.

D. Therapy and Prevention

Age-stratified data are needed on the efficacy, and frequency of side-effects, of current antibiotic therapies for infections. The risks vs. benefits of treating asymptomatic bacteriuria in older persons are not clear; prospective studies could contribute critical information. Since the relative prevalence of common pathogens in bacterial pneumonia and other infections of the elderly appears to depend in part on institutional setting and underlying diseases, the possibility of differences in optimal "empiric" antibiotic therapy for various subgroups of elderly patients needs examination.

Despite long-standing recommendations for influenza vaccination for the elderly, only about 20% of older persons receive immunization annually. Although the elderly account for the major share of tetanus-associated mortality in this country, a similar problem exists with low rates of immunization with tetanus toxoid. Studies on factors affecting the elderly's participation in vaccine programs could help to improve these rates.

The immune response to certain vaccines appears to be substantially impaired in many elderly. After vaccination, the time cause of antibody response, the persistence of effective titers, and the degree of protection conferred by a given titer may be altered with increasing age. Also, since the secondary response to many antigens may decrease less with age than the primary response, efficacy in the elderly of certain vaccines might be improved by primary immunization in early rather than later life. Evaluating the causes and degree of impaired response to vaccines in the elderly could help in improving immunization strategies and developing alternative prophylactic approaches.

Since risk for infections such as influenza and pneumonia varies widely among the elderly, efficacy studies on specific subpopulations (e.g., nursing home residents) could help improve targeting and cost-effectiveness evaluation of immunization and other prevention programs. The prevalence of nonvaccine serotypes in pneumococcal pneumonia in immunized and nonimmunized elderly populations needs close monitoring with regard to the future application and development of this vaccine. Other preventive measures, such as influenza vaccination for nursing home employees, need evaluation. The extent to which improved nutrition and ambulation may reduce infections in certain subgroups of elderly has not yet been thoroughly studied.

Other potential prevention strategies require preliminary studies: Optimal application in the elderly of new vaccines for viral and bacterial agents will depend on understanding age-related factors affecting pathogenesis and host response. Since T-cell function may be particularly impaired in older persons, the possibility that "T-independent" vaccines may be more effective in the elderly merits consideration. New techniques for production of pure antibody species suggest an increased potential role for passive immunization of the elderly, whose immune responses are commonly slowed. The possibility of preventing infections in the elderly by replacement therapy to correct immunologic deficits remains experimentally unexplored. In vitro assays of the effects of specific factors on human antiviral and antimicrobial cell function may be useful in preliminary studies on this question.

The above research areas illustrate the breadth of fertile topics for investigation; they are not intended to limit applications in any research area related to infectious diseases in the elderly. The NIA and NIAID are interested in all innovative research on the epidemiology, pathogenesis, diagnosis, prevention and treatment of this problem. A bibliography on infections in the elderly, developed by participants in an NIA/NIAID workshop on this topic, is available from the NIA and NIAID staff contacts listed at the end of this announcement.

III. MECHANISMS OF SUPPORT

Applications may be submitted for any of the conventional NIH grant support mechanisms, including the individual research project grant, program project, Clinical Investigator, New Investigator, Research Career Development, and Special Initiative Awards, and individual and institutional post-doctoral Research Service Awards (NRSAs). [1] (The NIAID will accept program project applications only in response to a specific Request for Applications and not as a result of this announcement.) The above list is not exhaustive; potential applicants are encouraged to communicate with the NIA and NIAID staff contacts listed at the end of this announcement regarding funding mechanisms and project design. Potential applicants for program project awards should contact NIA and NIAID staff very early in the planning stages.

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[1] NRSAs will be supported under the authority of the Public Health Service Act, Section 472, 42 USC 2891-1, and administered under PHS grants policy and Federal Regulation 42 CFR Part 66.

IV. APPLICATION AND REVIEW PROCEDURES

Applications should be submitted on PHS Form 398 (research grants), PHS Form 6025 (institutional NRSA) or PHS Forms 416-1, 416-2, and 416-3 (individual NRSA).

Applicants may obtain information and the appropriate application kits from their institution's grants office or by writing or calling:

Office of Grants Inquiries
Division of Research Grants
National Institutes of Health
Bethesda, Maryland 20205

Telephone: (301) 496-7441

Applicants are strongly encouraged to send a letter of intent to the NIA and NIAID staff contacts listed at the conclusion of this announcement at least 30 days before sending the completed application to the Division of Research Grants (address below). The letter of intent should include the title of the application, name of principal investigator and institutional address. If not, a brief abstract should be sent, followed as soon as possible by a copy of the completed application.

Applicants should enter the phrase "NIA/NIAID Program Announcement: Infectious Diseases in the Elderly" in response to Item 2 (Response to a Specific Program Announcement) on the first (face) page of their application. Applications should be submitted according to the deadlines for the appropriate review schedule and mailed to:

Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
Bethesda, Maryland 20205

One copy of the face page of the application should also be sent at this time to NIA and NIAID staff contacts listed at the end of this announcement. Applications will be reviewed for scientific merit either by an appropriate study section of the Division of Research Grants or by NIA or NIAID review committees, depending on the funding mechanism being sought. Review will be conducted in accordance with NIH policy and procedure involving peer review. Awards will be made on a competitive basis with all applications competing for NIA and NIAID funding.

V. APPLICATION RECEIPT DATES

For institutional and individual NRSAs, clinical investigator awards, senior fellowships, RCDAs, program projects, and competing continuations, the deadline dates are February 1, July 1, and October 1.

For new research grant applications not identified above, the deadline dates are March 1, July 1, and November 1.

VI. INQUIRIES AND CORRESPONDENCE

Correspondence, including requests for information, letters of intent, and advice should be directed to:

Evan Hadley, M.D.
Biomedical Research and Clinical
Medicine Program
National Institute on Aging
National Institutes of Health
Building 31 - Room 5C-21
Bethesda, Maryland 20205

Telephone: (301) 496-1033

and

Dr. John LaMontagne
Microbiology and Infectious
Diseases Program
National Institute of Allergy and
Infectious Diseases
National Institutes of Health
Westwood Building - Room 750
Bethesda, Maryland 20205

Telephone: (301) 496-7051

ANNOUNCEMENT

FUNDAMENTAL NEUROSCIENCES PROGRAM

NATIONAL INSTITUTE OF NEUROLOGICAL AND COMMUNICATIVE DISORDERS AND STROKE

Application Receipt Dates: March 1, July 1 and November 1

The Fundamental Neurosciences Program (FNP) of the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) is reissuing this program announcement designed to encourage the submission of applications for research grants in the neurophysiology of cognitive processes.

I. PURPOSE

This announcement is intended to stimulate new approaches to the experimental and conceptual aspects of research on those types of cognitive processes which can be studied at the neural level in both animal and human research. A primary goal should be to characterize the sources and time course of neural activity (where feasible in its relation to unit activity) related to these processes.

II. SCOPE

Projects of the following types illustrate this area:

A. Animal research:

1. Involving innovative methods and concepts for the definition and analysis of cognitive processes in experiments that are designed in response to new knowledge about the nervous system.
2. Applying recently established knowledge about cognitive processes in humans to the design of neurophysiological experiments in animals.
3. Requiring collaboration between scientists who are expert in the cognitive sciences and those who are expert in the neurobiological sciences.

This program is described in the Catalog of Federal Domestic Assistance,No. 13.854, Fundamental Neurosciences. Grants will be awarded under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended: 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems review.

B. Human research:

1. Developing new methods, concepts, and paradigms for research on cognitive processes that lead specifically toward studies of the underlying neural activities.

2. Applying recent advances in neurobiology to experiments using clinical neurophysiological and/or neuropsychological approaches to the study of cognitive processes.

3. Bringing experts in neurobiological research into collaboration with cognitive scientists.

III. APPLICATION AND REVIEW PROCEDURES

Applications should be prepared on form PHS 398 following instructions contained in the application kit. The applications will be judged solely on scientific merit in accord with NIH policy and procedures involving peer review. Initial review will be by the appropriate study section of the Division of Research Grants. The final review will be by the National Advisory Neurological and Communicative Disorders and Stroke Council. Applications judged more responsive to program interests of other Institutes will be assigned accordingly.

Deadline dates for the receipt of the applications are March 1, July 1, and November 1.

The phrase, "THE NEUROPHYSIOLOGY OF COGNITIVE PROCESSES," should be typed in Section 2 on the front page of the grant application form. The original and six copies of the application should be mailed to the following address:

Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
Bethesda, Maryland 20205

One copy of the application is to be sent to the address below. Also, for further information applicants may contact

Dr. W. Watson Alberts
Deputy Director
Fundamental Neurosciences Program
National Institute of Neurological
and Communicative Disorders and Stoke
Federal Building - Room 916
7550 Wisconsin Avenue
Bethesda, Maryland 20205

Telephone: (310) 496-1447

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11/13

NIH GUIDE for GRANTS and CONTRACTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Vol. 11, Nov. 13, December 13, 1982

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HAVE YOU MOVED?

If your present address differs from that shown on the address label, please send your new address to: Grants and Contract Guide Distribution Center, National Institutes of Health, Room B3BN10, Building 31, Bethesda, Maryland 20205, and attach your address label to your letter. Prompt notice of your change of address will prevent your name from being removed from our mailing list.

The GUIDE *is published at irregular intervals to announce scientific initiatives and to provide policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in grants and contracts activities administered by the National Institutes of Health.*

Two types of supplements are published by the respective awarding units. Those printed on yellow paper concern contracts: solicitations of sources and announcement of availability of requests for proposals. Those printed on blue paper concern invitations for grant applications in well-defined scientific areas to accomplish specific program purposes.

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ERRATA

BIOMEDICAL RESEARCH SUPPORT SHARED INSTRUMENTATION GRANTS

An Announcement in the November 5, 1982, NIH Guide for Grants and Contracts (Vol. 11, No. 12) entitled "Biomedical Research Support Shared Instrumentation Grants," Division of Research Resources, has the following errors:

1. Page 1 - Application Receipt Date should be: February 15, 1983.
2. Page 8 - The telephone number was omitted from the address of the Biomedical Research Support Grant Program. The telephone number should be: (301) 496-6743.
3. Page 8 - The last two-line paragraph on the page should be omitted.

FUNDAMENTAL NEUROSCIENCES: NEUROPHYSIOLOGY OF COGNITIVE PROCESSES

An Announcement in the November 5, 1982, NIH Guide for Grants and Contracts (Vol. 11, No. 12) printed on page 23, from the Fundamental Neurosciences Program, National Institute of Neurological and Communicative Disorders and Stroke, failed to include the title for this program. The title should be **"RESEARCH GRANTS IN THE NEUROPHYSIOLOGY OF COGNITIVE PROCESSES."**

NOTICE

CLINICAL CANCER EDUCATION

NATIONAL CANCER INSTITUTE

The Clinical Cancer Education Program announces that until new guidelines for the program are written and approved, no new and competing renewal applications will be accepted. At that time, the new guidelines together with information on the receipt dates for applications will be published.

NOTICE

REVISED PHS GRANTS POLICY STATEMENT NOW AVAILABLE

The revision of the Public Health Service Grants Policy Statement is now available. The successor to the October 1, 1976 issuance is designated as DHHS Publication No. (OASH) 82-50,000 (Rev.) December 1, 1982. The Public Health Service has sent one free copy to each grantee institution of record addressed to: "Director, Office of Research Program Support." NIH hopes to make some limited additional distribution; however, institutions or individuals desiring additional copies may obtain them for $5.00 each by writing to:

Superintendent of Documents
U.S. Government Printing Office
Washington, D.C. 20402

In addition to the DHHS Publication Number referenced above, requests should include the GPO Stock No. 017-020-00090-01 to expedite delivery.

Questions of interpretation, clarification, or correction will be provided as necessary in subsequent issuances of this Guide or other official communications.

REMINDER NOTICE

DEADLINE FOR SUBMISSION OF ASSURANCES OF COMPLIANCE WITH REVISED HUMAN SUBJECTS PROTECTION REGULATIONS

On January 26, 1981, the Department of Health and Human Services (DHHS) published final regulations amending basic DHHS policy for the protection of human research subjects. Institutions holding an Assurance of Compliance were encouraged to implement new provisions of the regulations prior to the negotiation of a revised Assurance of Compliance. Since August, 1981, the Office for Protection from Research Risks (OPRR) has been negotiating Assurances of Compliance with the new regulations.

This notification is to remind institutions of the December 31, 1982 deadline, for submission of a general (Multiple Project) assurance prepared in accord with DHHS regulations published in the Federal Register on January 16, 1981 (46 FR 8366).

Institutions are encouraged to submit an Assurance of Compliance at the earliest possible date. A sample assurance is available from OPRR (301 - 496-7041). Although it is possible that approval of a multiple project assurance might not be transmitted until sometime after December 31, 1982, institutions may continue to function under their former assurance until such time as approval for the revised assurance is given. Special (Single Project) assurances will continue to be approved on a single project basis. GENERAL ASSURANCES WHICH HAVE NOT BEEN REVISED TO MEET THE 1981 REQUIREMENTS AND SUBMITTED TO OPRR WILL BE TERMINATED EFFECTIVE JANUARY 1, 1983.

NOTICE

CELL CULTURE IDENTIFICATION SERVICE

NATIONAL CANCER INSTITUTE

This announcement is being issued to inform investigators of the availability of a service for the inter- and intra-species identification of cell cultures.

The Biological Carcinogenesis Branch (BCB), Carcinogenesis Extramural Program, National Cancer Institute (NCI), has a continuing interest in the proper characterization of established cell lines. Therefore, the BCB has supported under contract N01-CP-21017 with the Children's Hospital of Michigan a service facility to aid in confirming or establishing species and intraspecies identity of cell cultures. This service, available to all interested investigators, uses species specific immunofluorescence, isoenzyme analysis, and cytogenetic examination.

Evaluation of cell cultures with species-specific antisera can rapidly identify the species of the cell line and determine whether more than one cell species is present. Isozyme analysis confirms species determination. Multiple polymorphic isozymes are helpful in precisely identifying human cell lines. Chromosomal analysis, using banding techniques, denotes chromosome numbers and markers that uniquely distinguish among cell lines. These examinations also contribute to information about changes in cultures that may have resulted from experimental manipulation. During the past several years, this cell monitoring service has proven useful to many investigators because it has provided critical information to them about the current status of their cell lines. It has also been useful in detecting cell contamination problems.

A modest service fee is charged that covers partial costs for the work done. The fee schedule is available upon request.

Investigators interested in making use of this service should contact:

Dr. Ward D. Peterson, Jr.
Child Research Center
Children's Hospital of Michigan
3901 Beaubien Boulevard
Detroit, Michigan 48201

Telephone: (313) 494-5570

NOTICE

TEACHING NURSING HOME (TNH) AWARD

NATIONAL INSTITUTE ON AGING

Prospective applicants for the National Institute on Aging (NIA) Teaching Nursing Home (TNH) award are advised that the TNH award has been changed to a Program Project (P01) support mechanism. This change requires that applications for the TNH program project award be limited to a total of $500,000 for direct costs, including core support not to exceed $125,000.

Supplementary information is available on preparation of applications for the TNH under program project guidelines. Requests for information on TNH applications may be obtained from:

Noel D. List, M.D., M.P.H.
National Institute on Aging
National Institutes of Health
Building 31 - Room 5C-21
Bethesda, Maryland 20205

Telephone: (301) 496-6761

ANNOUNCEMENT

PARTICIPANTS SOUGHT FOR NATIONAL COOPERATIVE

DRUG DISCOVERY GROUPS

DIVISION OF CANCER TREATMENT

NATIONAL CANCER INSTITUTE

Chemotherapy has had a major impact on the cure of cancer over the past two decades. Nevertheless, there is considerable need for the discovery of new and more efficacious agents with higher therapeutic ratios for the treatment of these diseases. Many exciting leads in fundamental science are available for possible exploration and possible extrapolation into new drug classes with unique mechanisms of action, and new approaches to control cancer. Considerable research talent is available nationally that could be employed in a very effective manner. However, to accomplish this requires a national support mechanism that would permit the most outstanding investigators in chemistry, biology, biochemistry and pharmacology (all needed for effective drug discovery) to interact in a manner that leads to the efficient invention of new strategies and entities for the treatment of cancer. Since it is clear that few single institutions possess a critical mass of all of the varied talents needed for effective drug discovery, a new instrument that permits the combination of the available expertise from diverse institutions is required. These units, termed National Cooperative Drug Discovery Groups (NCDDG) are envisioned to have the capacity to generate new approaches to therapeutic inventions, to rapidly translate their concepts into new chemical entities, to conduct adequate and unique biological evaluations, and to carry out in-depth biochemical and pharmacological studies. It is expected that the NCDDG, because of their unique ability to apply highly sophisticated multi-disciplinary technologies in concert, will discover and bring new entities to a pre-clinical stage that will allow the most enlightened use of other DCT resources for rapid development and clinical evaluation.

The Developmental Therapeutics Program (DTP), Division of Cancer Treatment (DCT), National Cancer Institute (NCI) is proposing to establish the NCDDG. The goal of the NCDDG will be the discovery of new, clinically effective anticancer agents. While the compounds investigated may have synthetic, natural product or semi-synthetic origins, all proposed projects must have a strong scientific rationale. As currently envisioned, the basic scientific composition of a NCDDG would consist of programs in at least four scientific disciplines: chemistry, biology, biochemistry and pharmacology. The Groups would be organized under a Group Director (Principal Investigator) who will assemble a multi-institutional group of Program Leaders. This Group would contain the diversity of outstanding scientific skills needed to conduct a vigorous and effective new drug discovery effort. Emphasis will be on new structural types rather than analogs of known active compounds. The ultimate accomplishments of a NCDDG will, in large measure, depend on the skill of the Group Director in identifying likely targets for this effort and in blending the work of multiple scientific leaders toward a common goal. After formation of a NCDDG, it is intended that DTP will interact closely with the Groups. DTP will be responsible for the development (formulation, toxicology) of successful drug candidates to clinical trial.

The purpose of this initial announcement is to allow outstanding scientists who are interested in participating as a Group Director (i.e., Principal Investigator responsible for group formation, proposal preparation, and overall administration of the Group) or Program Leader (chemistry, biology, etc., see above) to identify themselves. It is the intention of DTP to tabulate and distribute this information within 30 days of announcement closing to all who respond to this announcement. This should help compatible scientists form strong, multi-institutional groups for the submission of applications which address this approach to anticancer drug discovery. Proposals that include more than 50% of the effort from a single campus or organization are discouraged. This announcement is intended only to expedite the formation of the groups. The DCT plans to issue a Request for Application (RFA) outlining the specifics of the NCDDG Program. Such an RFA will not be restricted to respondents to this announcement. The NCI will play no role in the formation of the Groups other than to distribute the information described above. The final composition of applicant groups may include respondents to this announcement or other scientists expressing interest at a later date.

Leading scientists from academia, research institutions and industry who are interested in leading or participating in a NCDDG should submit ONLY the following information which will be tabulated and sent to investigators supplying information:

Name
Institution (including Department, mailing address and telephone number)
Scientific discipline (Chemistry, Biology, Biochemistry, Pharmacology, Other)
Participation level interest (Group Director and/or Program Leader)

This information should be sent by January 17, 1983 to:

Dr. John M. Venditti
Chief, Drug Evaluation Branch
Developmental Therapeutics Program
Division of Cancer Treatment
National Cancer Institute
National Institutes of Health
Blair Building - Room 428
8300 Colesville Road
Silver Spring, Maryland 20910

Telephone: (301) 427-8703

NOTICE

REQUEST FOR APPLICATIONS (RFA) AVAILABLE

SIDE EFFECT ASSESSMENT IN PSYCHOPHARMACOLOGIC CLINICAL TRIALS

PUBLIC HEALTH SERVICE
ALCOHOL, DRUG ABUSE, AND MENTAL HEALTH ADMINISTRATION
NATIONAL INSTITUTE OF MENTAL HEALTH

Application Receipt Date: March 1, 1983

As part of its mission to stimulate and support treatment assessment research for pharmacologic and somatic therapies of mental disorders, the Pharmacologic and Somatic Treatments Research Branch (PSTRB), National Institute of Mental Health (NIMH) has sought to improve the methodology and techniques available to assess these therapies. Assessment of adverse consequences (side effects) in clinical trials of psychotropic drugs has lagged significantly behind measurement of the intended therapeutic effects (efficacy) of these agents. In recognition of these problems, PSTRB, NIMH, initiated a program to develop methodology for the assessment of adverse consequences of psychotropic drugs in the context of clinical trials.

A technique for rating adverse drug reactions, Systematic Assessment for Treatment Emergent Events (SAFTEE), has been developed and tested for feasibility in clinical trial settings. The rating system includes both elicitation procedures and a recording form on which to report the information elicited about the events at each examination. There are two distinct levels of elicitation, "General Inquiry" and "Systematic Inquiry," each with specific examination procedures.

The purpose of this Request for Applications (RFA) is to invite applications to investigate systematically the reliability, validity, and characteristics of the new methodology when used in clinical trials under a range of conditions, specifically when used with various patients populations, different pharmacologic agents, raters representing different disciplines, and varying options for assessment called for by study protocols.

Copies of the complete Request for Applications, SAFTEE and additional information may be obtained from Jerome Levine, M.D., Chief, or Nina R. Schooler, Ph.D., Assistant Chief, at the following address:

Pharmacologic and Somatic Treatments
   Research Branch
National Institute of Mental Health
Parklawn Building - Room 10C-06
5600 Fishers Lane
Rockville, Maryland 20857

Telephone: (301) 443-3524

Applications for this specific funding initiative should be submitted by the March 1, 1983 receipt date.

ANNOUNCEMENT

SMALL GRANTS FOR OCCUPATIONAL SAFETY AND HEALTH RESEARCH

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
CENTERS FOR DISEASE CONTROL
NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH

The National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control (CDC), announces that competitive grant applications for small grants to support occupational safety and health research will be accepted until January 3, 1983.

I. PURPOSE

This NIOSH Small Grant Program invites applications for research grants covering scientific areas relevant to occupational safety and health and is intended to provide financial support for investigators who do not have Federal or non-Federal research grant support. The grants may be used to carry out exploratory or pilot studies, to develop or test new techniques or methods, or to analyze data previously collected. Examples of programmatic areas of interest are traumatic injuries, reproductive effects, neurologic and cardiovascular effects, occupational respiratory diseases, occupational cancers, musculoskeletal injuries, noise-induced hearing loss, dermatologic problems, and psychologic disorders. Potential applicants with questions concerning the acceptability of their proposed work should contact the individuals listed in this announcement.

II. AUTHORITY

These grants will be awarded and administered by NIOSH under the research and demonstration grant authority of section 20(a)(1) of the Occupational Safety and Health Act of 1970 (29 U.S.C. 669(a)(1)) and section 501 of the Federal Mine Safety and Health Act of 1977 (30 U.S.C. 951). Program regulations applicable to these grants are contained in Part 87 of Title 42, Code of Federal Regulations, "National Institute for Occupational Safety and Health Research and Demonstration Grants." Except as otherwise indicated, the basic grant administration policies of the Public Health Service are applicable to this program. Applications responsive to this announcement are not subject to OMB Circular A-95 Clearinghouse and/or Health Systems Agency review. This program is described in the Catalog of Federal Domestic Assistance No. 13.262, Occupation Safety and Health Research Grants.

III. ELIGIBLE APPLICANTS

This program is intended primarily for predoctoral graduate students and postdoctoral researchers; however, investigators from any scientific discipline and at any stage of their careers may apply for these grants.

Support under this program may not be requested to supplement research projects receiving Federal or non-Federal support or to provide interim support of projects under review by the Public Health Service. A grant application responsive to this announcement, submitted simultaneously with a regular research grant application on the same topic, will not be accepted.

IV. AVAILABILITY OF FUNDS

The total grant award may comprise direct costs of up to $15,000 per year and additional indirect costs, as appropriate. The grants may be awarded for up to two years and will not be renewable. It is anticipated that the total annual amount available for grants under this program will be $300,000. The specific amount to be funded will, however, depend upon the merit and scope of the applications received and the availability of funds. Grantees will be required to cost share a minimum of 5 percent.

V. ALLOWABLE EXPENSES (direct costs)

Support may be requested for the following categories:

1. Supplies.
2. Travel to attend a domestic meeting or visit another laboratory for the purpose of gathering more information or to learn a new technique or procedure relevant to the application. Relevance and importance must be justified in the applications.
3. Small items of equipment. The purchase of large equipment is discouraged.
4. Salary for technical personnel. Salary of the principal investigator will be allowed only with strong justification.

VI. CRITERIA FOR REVIEW

Applications will be reviewed by an appropriate scientific review group on the basis of scientific merit and significance of the project, scientific competence of the proposed principal investigator and supporting faculty (where appropriate) in relation to the type of research involved, feasibility of the project, likelihood of its producing meaningful results, appropriateness of the proposed budget, adequacy of the applicant's resources available for the project, and the supportive nature of the research environment. For those applications from students, the review process will take into consideration the fact that the applicants do not have extensive experience with the grant process.

VII. APPLICATION AND AWARD

Applications should be submitted on form PHS 398 (Rev. 5/80), available at most institutional business offices. Application kits may also be obtained from:

Office of Grants Inquiries
Division of Research Grants
National Institutes of Health
Westwood Building - Room 448
5333 Westbard Avenue
Bethesda, Maryland 20205

Telephone: (301) 496-7441

Care should be taken in following the instructions included with the application form, making certain to address the points identified under the heading "REVIEW CRITERIA."

An original and six copies of the application must be received no later than January 3, 1983, in order to be considered in the February/March 1983 Study Section meeting. Completed applications must be sent or delivered to:

Application Receipt Office
Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205

A brief covering letter should accompany the application indicating that it is submitted in response to this announcement.

Applicants may meet the deadline by either delivering or mailing the application on or before the above specified date provided the following conditions are met:

A. Mailed applications. Applications mailed through the U.S. Postal Service will be considered as meeting the deadline if they are either:

   1. Received on or before the deadline date at the Division of Research Grants, NIH, or

   2. Sent by first class mail, postmarked on or before the deadline date, and received by the granting agency in time for submission to the independent review group. (Applicants are cautioned to request a legible U.S. Postal Service postmark or to use express mail or certified mail and to obtain a legible dated mailing receipt from the U.S. Postal Service. Private metered postmarks will not be acceptable as proof of timely mailing.)

B. Applications submitted by other means. Applications submitted by any means except mailing first class through the U.S. Postal Service will be considered as meeting the deadline only if they are physically received at a place specified above before close of business on or before the deadline date.

C. Late applications. Applications which do not meet the criteria in either paragraph 1. or 2. are considered late applications. In that event, an application will not be considered in the current competition and will be returned to the applicant.

It is anticipated that awards will be made as early as May 1, 1983.

VIII. FOR FURTHER INFORMATION CONTACT:

Jack E. McCracken, Ph.D.
Acting Chief, Grants Administration and Review Branch
Parklawn Building - Room 8-63
5600 Fishers Lane
Rockville, Maryland 20857

Telephone: (301) 443-4496

or

Mr. Joseph West
Grants Management Officer, NIOSH
Parklawn Building - Room 8-23
5600 Fishers Lane
Rockville, Maryland 20857

Telephone: (301) 443-3122

ANNOUNCEMENT

AVAILABILITY OF REQUESTS FOR APPLICATIONS (RFA)

DIVISION OF HEART AND VASCULAR DISEASES
NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

CORONARY ARTERY REACTIVITY, INJURY AND THROMBOSIS

Application Receipt Date: April 15, 1983

The Cardiac Diseases Branch, Division of Heart and Vascular Diseases, National Heart, Lung, and Blood Institute (NHLBI) expects to publish a Request for Applications (RFA) on the above subject, on or about December 31, 1982. Copies of this RFA are currently available from staff of the NHLBI.

This program will support basic research on coronary artery spasm and coronary thrombosis as contributing factors to myocardial infarction and rest angina. Projects should be focused on the biology and pathophysiology of coronary arteries in the context of spasm and thrombosis. Also of interest are the effects which spasm may have in contributing to the formation of an occlusive thrombus and conversely the effects the metabolic products of a thrombus may have in inducing spasm. This announcement may be of particular interest to investigators with expertise in coronary physiology, rheology, hematology, coagulation, biochemistry, pathology, immunology, pharmacology and electrophysiology.

Request for copies of the RFA should be addressed to:

Constance Weinstein, Ph.D.
Deputy Chief, Cardiac Diseases Branch
National Heart, Lung, and Blood Institute
Federal Building - Room 312
7550 Wisconsin Avenue
Bethesda, Maryland 20205

Telephone: (301) 496-1081

DYSRHYTHMIAS IN THE DEVELOPING AND IMMATURE HEART

Application Receipt Date: April 15, 1983

The Cardiac Diseases Branch, Division of Heart and Vascular Diseases, National Heart, Lung, and Blood Institute (NHLBI) expects to publish a Request for Applications (RFA) on the above subject on or about December 31, 1982. Copies of this RFA are currently available from staff of the NHLBI.

This program will support research on basic developmental electrophysiology and on control of dysrhythmias in the young. Fundamental studies of how development influences impulse generation, conduction and mechanisms of reentry are appropriate. Also of interest are studies which elucidate the differences between immature and adult cardiac tissues in their responses to pharmacologic interventions. Projects may involve studies on cells, animal models and/or patients. However, clinical trials on clinical drug validation studies would not be responsive to the request. This announcement may be of particular interest to investigators with expertise in embryology, physiology, pharmacology, biophysics and electrophysiology.

Request for copies of the RFA should be addressed to:

Zena McCallum
Cardiac Diseases Branch
National Heart, Lung, and Blood Institute
Federal Building - Room 3C-06
7550 Wisconsin Avenue
Bethesda, Maryland 20205

Telephone: (301) 496-1081

BIOBEHAVIORAL FACTORS AFFECTING HYPERTENSION IN BLACKS

Application Receipt Date: April 15, 1983

The Behavioral Medicine Branch, Division of Heart and Vascular Diseases, National Heart, Lung, and Blood Institute (NHLBI) expects to publish a Request for Applications (RFA) on or about December 31, 1982. Copies of this RFA are currently available from staff of the NHLBI.

This program will support research to gain basic information of possible blood pressure and other physiological differences between Black and White populations in response to specific behavioral/psychological stressors. The proposed research must address the interaction of selected behavioral and physiological variables relevant to the development of hypertension among population subgroups. This announcement may be of particular interest to investigators with interdisciplinary expertise in studies of cardiovascular responses to controlled psychological stimuli.

Request for copies of the RFA should be addressed to:

Dr. Katrina W. Johnson
National Heart, Lung, and Blood Institute
Federal Building - Room 604
7550 Wisconsin Avenue
Bethesda, Maryland 20205

Telephone: (301) 496-9380

CARDIAC HYPERTROPHY AND FAILURE IN CHRONIC HYPERTENSION

Application Receipt Date: April 15, 1983

The Hypertension and Kidney Diseases Branch, Division of Heart and Vascular Diseases, National Heart, Lung, and Blood Institute (NHLBI) expects to publish a Request for Applications (RFA) on the above subject on or about December 31, 1982. Copies of this RFA are currently available from staff of the NHLBI.

This program will support a broad range of new research projects seeking to characterize the transition from normal cardiac structure and function to cardiac hypertrophy and cardiac failure in experimental models with chronic hypertension. The range includes the attendant hemodynamic, morphological, histological, physiological, and biochemical changes affecting stromal, muscular, and vascular components of the heart, as well as identification of points in the process where changes are "reversible" and where they are "irreversible."

Letters of intent are encouraged to be submitted by February 15, 1983. Request for copies of the RFA should be addressed to:

Dr. John B. Dunbar
National Heart, Lung, and Blood Institute
Federal Building - Room 4C08
7550 Wisconsin Avenue
Bethesda, Maryland 20205

Telephone: (301) 496-1857

ANNOUNCEMENT

PREVENTIVE CARDIOLOGY ACADEMIC AWARD

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Application Receipt Date: April 1, 1983

I. BACKGROUND

A. The Division of Heart and Vascular Diseases of the National Heart, Lung, and Blood Institute (NHLBI), has initiated the Preventive Cardiology Academic Award to provide a stimulus for the development of a preventive cardiology curriculum in those schools of medicine and osteopathy that do not have one and to strengthen and improve the preventive cardiology curriculum in those schools that do. Each school of medicine or osteopathy in the United States and its possessions or territories is eligible to compete for one award for a project period that does not exceed five years. The number of awards made each year will depend upon the merit of the applications received and availability of funds.

II. PURPOSE

A. For the purposes of the Preventive Cardiology Academic Award, the term preventive cardiology is used to define the area of cardiovascular medicine having a special concern with the development of knowledge and the application of knowledge directed at the prevention of heart and vascular diseases. This includes the area of primary prevention of cardiovascular diseases in infants, children, and adults who are at risk of developing such diseases and the reduction of preventable complications or disability in persons who have already developed cardiovascular disease.

B. This award is intended to:

1. Encourage the development of a high quality preventive cardiology curriculum in schools of medicine and osteopathy that will significantly increase the opportunities for students and house staff to learn both the principles and practice of preventive cardiology.

2. Develop promising faculty whose interest and training are in preventive cardiology teaching, research, and practice.

This program is described in the Catalog of Federal Domestic Assistance No. 13.837, Heart and Vascular Diseases Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410 as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

3. Develop established faculty who have a major commitment to and possess educational skills for teaching preventive cardiology.

4. Facilitate interchange of educational ideas and methods applicable to teaching preventive cardiology among awardees and institutions.

5. Develop at the grantee institution the ability to strengthen continuously the improved preventive cardiology curriculum, with local funds, subsequent to the award.

III. CRITERIA FOR THE AWARD

Competitive review of proposals will include an evaluation of the evidence of commitment of both the sponsoring institution and the head of the cardiology division to the accomplishment of the objectives of the award as well as the qualifications, interest and commitment of the candidate to undertake responsibility for implementing a high quality preventive cardiology curriculum. Sponsorship of the candidate must be by the head of the division responsible for the teaching and practice of cardiology in the institution. Joint appointments with other departments or schools such as Preventive Medicine, Pediatrics or Epidemiology are encouraged when they would lead to a meaningful enhancement of the curriculum, extend concepts of prevention to other teaching areas or enhance the candidate's professional development in preventive cardiology teaching, research or practice. Multidisciplinary programs are encouraged.

The candidate must have sufficient clinical training and research experience in cardiology to be able to develop and implement a high quality curriculum within the institution. If the candidate's background requires further educational development, the plans to acquire this additional training should be described. Relevant training in epidemiology, clinical trials, behavioral science or other areas could be advantageous in the broader role of the candidate in stimulating preventive cardiology concepts among other health professionals in the institution.

IV. PROVISIONS OF THE AWARD

The non-renewable Preventive Cardiology Academic Award will include funds for the awardee's salary, fringe benefits, funds for curriculum development, and actual indirect costs not to exceed 8% of total allowable direct costs.

The applicant may request salary support up to $30,000 per year. In addition to this amount, fringe benefits may be requested at the applicable institutional rate.

The applicant must devote a minimum of 50% time to this grant and the salary which is requested may not exceed the time or effort to be devoted to the Preventive Cardiology Academic Award. The total salary on which it is based must be consistent both with the established salary structure at the institution and with salaries actually provided by the institution from its own funds to other staff members of equivalent qualifications, rank, and responsibilities in the department concerned. If full-time salaries are not currently paid to comparable staff members, the proposed salary must be appropriately related to the existing part-time salary structure. The awardee may devote up to 50% effort as principal or participating investigator on an NIH-supported grant(s) or contract(s) and may be remunerated from the grant(s) or contract(s) accordingly.

Developmental funds may include personnel support necessary to achieve the program objectives; travel funds to enable the awardee to visit other institutions or to attend special meetings, courses or conferences designed to increase his/her knowledge and competence in the teaching/learning process related to preventive cardiology; equipment necessary as teaching aids; supplies necessary to the program objectives; and stipends for a limited number of students to extend their preventive cardiology learning experience during their elective quarter in the academic year. Funds may not be used to support cardiology fellowships or research projects.

V. REVIEW OF APPLICATIONS

Applications for initial Preventive Cardiology Academic Awards will be appraised in terms of criteria outlined for the institution and the awardee in Criteria for the Award.

The review will include an initial assessment of the written proposal and an interview with the prospective awardee in Bethesda, Maryland, by the Research Manpower Review Committee managed by the Division of Extramural Affairs of NHLBI. (Travel expenses for this interview must be paid by the applicant institution.) When necessary, a site visit may be made to the institution to determine the institutional environment, the commitment of the sponsoring division or department head and evidence of cooperation that may be needed to implement the candidate's proposed program. The Research Manpower Review Committee will recommend applications for consideration to the National Heart, Lung, and Blood Advisory Council.

VI. METHOD OF APPLYING

Each prospective applicant is encouraged to forward a brief letter of intent, countersigned by the head of the cardiology division or department, by March 1, 1983, to:

Dr. Carol Letendre
Contracts, Clinical Trials, and
  Training Review Section
National Heart, Lung, and Blood Institute
Westwood Building - Room 548
Bethesda, Maryland 20205

These letters will not be considered commitments but will be used to estimate the number of proposals to be submitted.

Applications for Preventive Cardiology Academic Awards may be submitted for the April 1, 1983, receipt date to the National Institutes of Health (NIH) for review by the National Heart, Lung, and Blood Advisory Council in September 1983. The requested beginning date for funding should be July 1, 1984.

Application form PHS 398 (Rev. 5/80) may be obtained from the administrative office of the applicant institution or from the Division of Research Grants (DRG), NIH.

Deadline for receipt of applications:

Application Receipt	Council Review	Start Date
April 1	September	July 1*

* Of the year following application receipt.

VII. FOR ADDITIONAL INFORMATION

Prospective applicants are encouraged to review the Preventive Cardiology Academic Awards Guidelines dated December 1, 1982, which detail the eligibility requirements and application procedures. Requests for copies of these Guidelines and questions related to the Preventive Cardiology Academic Award should be directed to:

Dr. William T. Friedewald
Acting Chief, Preventive Cardiology Branch
Clinical Applications and Prevention Program
Division of Heart and Vascular Diseases
National Heart, Lung, and Blood Institute
Federal Building - Room 212A
Bethesda, Maryland 20205

Telephone: (301) 496-2533

ANNOUNCEMENT

IMMUNOHISTOCHEMICAL CLASSIFICATION OF SOLID TUMORS

NATIONAL CANCER INSTITUTE

Application Receipt Dates: March 1, July 1, and November 1

Immunohistochemical techniques, such as immunoperoxidase and immunofluorescence, are available that allow the examination of fixed or frozen tissue from biopsies, surgical specimens and autopsy material. The techniques provide the opportunity for a systematic attempt at the identification of antigens within or on the surface of tumors.

The Diagnosis Program is actively interested in tumor-associated substances as markers with several uses. Frequently serum and urine obtained at the time of initial diagnosis or before initiation of treatment are not available, whereas fixed or frozen tissue is usually a permanent feature which is available for most cancers. Therefore the analysis of fixed or frozen tissue may provide insight into which markers are best for monitoring therapy in addition to predicting response to therapy. There is the need for a systematic and thorough examination of different solid tumors to catalog the variety of antigens present and to relate as many of these antigenic characteristics as possible to the clinical features of that type of cancer.

The purpose of this announcement is to stimulate immunohistochemical classification attempts since many laboratories are performing the tests but may not have adequate support for a careful retrospective correlation of immunohistochemical staining with the clinical features in a large number of patients.

Investigators are invited to submit applications to employ immunohistochemical techniques to examine fixed or frozen tissues from biopsies, surgical specimens and autopsy material to establish retrospective correlation with clinical features which may provide indications for immunochemical markers that can aid in determining prognosis, selection of therapy, detection of early recurrent tumor, etc. The description of tumor cells by functional characteristics in addition to traditional morphologic and chemical staining patterns could lead to new classification schemes that would provide more information relative to the clinical picture.

This program is described in the Catalog of Federal Domestic Assistance No. 13.396, Cancer Biology. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

METHOD OF APPLYING

Applications should be submitted on form PHS-398 (Rev. 5/80), which is available in the grants and contracts business office at most academic and research institutions or from the Division of Research Grants (DRG), National Institutes of Health (NIH). Review and award of the successful applications will be through the usual NIH procedures governing research project grants. The phrase "PREPARED IN RESPONSE TO PROGRAM ANNOUNCEMENT: IMMUNOHISTOCHEMICAL CLASSIFICATION OF SOLID TUMORS" should be typed under item 2 on page 1.

In addition a brief covering letter should accompany the application indicating it is being submitted in response to this program announcement. The original and six copies of the application should be sent or delivered to:

Applications Receipt Office
Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
Bethesda, Maryland 20205

For further information, investigators are encouraged to contact:

K. Robert McIntire, M.D.
Chief, Diagnosis Branch
Program Director, Diagnosis Program
Division of Cancer Biology and Diagnosis
National Cancer Institute
Building 31 - Room 3A10
Bethesda, Maryland 20205

Telephone: (301) 496-1591

In order to alert the Diagnosis Program to the submission of applications in response to this announcement, a copy of the covering letter should be sent to Dr. McIntire.

ANNOUNCEMENT

DEVELOPMENT OF MYELOMA OR HUMAN B CELL LINES SUITABLE FOR SOMATIC CELL HYBRIDIZATION TO PRODUCE HUMAN MONOCLONAL ANTIBODIES

NATIONAL CANCER INSTITUTE

Application Receipt Dates: March 1, July 1, November 1

The National Cancer Institute (NCI) invites applications for support of research related to establishing human myeloma or B cell lines appropriate for use in monoclonal antibody production.

The fusion of mouse myeloma cells in continuous culture with immunized mouse spleen cells to produce hybrid cells each producing a single monospecific antibody was accomplished by Kohler and Milstein in 1975 and has revolutionized immunology. The fact that these hybrids are capable of being propagated indefinitely in tissue culture or as a transplantable tumor in histocompatible mice, has made possible the production of unlimited amounts of monoclonal antibodies with selected specificity.

There has been great interest in applying these monoclonal antibodies to the clinical problems of cancer management for immunodiagnosis, immunolocalization and immunotherapy. For in vivo use in human patients with or suspected of having cancer there are obvious advantages in utilizing human monoclonal antibody rather than one of mouse or rat origin.

The human myeloma and B cell lines that are currently available for fusion with human immune B lymphocytes have not shown the efficiency in fusion, cloning and antibody synthesis that is obtainable with the available mouse myeloma lines. For this reason, the NCI is interested in stimulating the development of human cell lines of plasma cell or B lymphocyte origin that are capable of serving as fusion partners for the production of human-human hybridomas synthesizing human monoclonal antibody. Special attention should be given to cell lines that are non-secretors of immunoglobulin and are not contaminated by viral infection.

Investigators able to conduct the above studies are encouraged to submit a grant application to the Division of Research Grants (DRG).

This program is described in the Catalog of Federal Domestic Assistance No. 13.396, Cancer Biology. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

METHOD OF APPLYING

Applications should be submitted on form PHS-398 (Rev. 5/80), which is available in the grants and contracts business office at most academic and research institutions or from the Division of Research Grants, National Institutes of Health (NIH). Review and award of the successful applications will be through the usual NIH procedures governing research project grants.

The phrase "PREPARED IN RESPONSE TO PROGRAM ANNOUNCEMENT: DEVELOPMENT OF MYELOMA OR HUMAN B CELL LINES SUITABLE FOR SOMATIC CELL HYBRIDIZATION TO PRODUCE HUMAN MONOCLONAL ANTIBODIES" should be typed under item 2 on page one of the application.

In addition, a brief covering letter should accompany the application indicating it is being submitted in response to this program announcement. The original and six copies of the application should be sent or delivered to:

Applications Receipt Office
Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
Behesda, Maryland 20205

For further information, investigators are encouraged to contact:

K. Robert McIntire, M.D.
Chief, Diagnosis Branch
Program Director, Diagnosis Program
Division of Cancer Biology and Diagnosis
National Cancer Institute
Building 31 - Room 3A10
Bethesda, Maryland 20205

Telephone: (301) 496-1591

In order to alert the Diagnosis Program to the submission of applications in response to this announcement, a copy of the covering letter should be sent to Dr. McIntire.

ANNOUNCEMENT

RESEARCH GRANTS ON HORMONES AND EPILEPSY

NATIONAL INSTITUTE OF NEUROLOGICAL AND COMMUNICATIVE DISORDERS AND STROKE

Application Receipt Dates: March 1, July 1, November 1

I. INTRODUCTION

The Epilepsy Branch, Neurological Disorders Program of the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) encourages the submission of research grant applications (R01) on the role of hormones in epilepsy.

II. BACKGROUND

Even though there is a large and ever increasing amount of information on endocrine-brain relationships, the role of hormones in epilepsy is not well defined. It is becoming obvious that hormones can significantly alter brain activity either through excitatory or inhibitory mechanisms. Conversely, there is a growing body of evidence that indicates seizures and antiepileptic drugs can influence hormonal balance.

A number of hormones influence maturation of mammalian brain. Thyroid insufficiency during early development may result in increased brain excitability secondary to delays in maturation of inhibitory neuronal activity. A variety of adverse conditions may lead to changes in endocrine function with delays in brain development, which may lead to epilepsy. In the adult brain, hormones may influence epilepsy by altering excitability of cortical or limbic regions. Ovarian hormones and thyroid hormones appear to have direct effects on CNS excitability. Thyroid hormones influence the synthesis of neurotransmitters and alter receptor sensitivity. Glucocorticoids enhance the activity of enzymes in the synthesis of monoamines.

Seizures and antiepileptic drugs can have significant influences on hormonal balance. Phenytoin has been shown to increase the rate of release of glucocorticoids and antagonizes the effects of parathyroid hormone on calcium metabolism. Mean levels of a number of hormones including prolactin, cortisol and cholesterol have been shown to be elevated in epileptic patients, possibly due to an alteration in neurotransmitter activity during the seizure.

This program is described in the Catalog of Federal Domestic Assistance No. 13.854, Fundamental Neurosciences. Grants will be awarded under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

Studies done to date indicate a relationship between hormones and epilepsy. Further research is needed to determine the basic physiological processes by which hormones influence seizure generation and spread, and how hormonal state can influence brain development and seizure susceptibility.

III. RESEARCH GOALS

Research grant applications should focus on the basic neurophysiology and endocrinology involved in the proconvulsant or anticonvulsant activity of hormones, as well as the effects of seizure activity on hormonal states. Related research supporting this effort would be appropriate. The primary research goals are: 1) to determine the influence of various hormones on brain development and generation of epileptiform discharges; 2) to determine the underlying physiological processes whereby hormones influence seizure generation and spread; and 3) to determine the influence of seizures and antiepileptic drugs on hormonal states.

IV. MECHANISM OF SUPPORT

Support for this program will be through the regular research project grant. Each successful applicant will plan, direct, and carry out the individual research project.

V. APPLICATION AND REVIEW PROCEDURES

Applications should be prepared on form PHS 398 (Rev. 5/80) following instructions contained in the application kit. Application kits are available from most institutional business offices, or may be obtained from the Division of Research Grants, at the address given below.

Applications must be responsive to the program announcement and the goals of NINCDS. They will be judged on scientific merit and program relevance in accordance with NIH policy and procedures involving peer review. An initial review will be made by the appropriate study section of the Division of Research Grants. A second level review will be made by the National Advisory Neurological and Communicative Disorders and Stroke Council.

Application receipt dates are: March 1, July 1 and November 1.

The phrase "NINCDS Program Announcement on Hormones and Epilepsy" should be typed in space No. 2 of the face page of the application. The original and six copies of the application should be mailed to:

Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205

One copy of the application is to be sent to the addressee below. Also, for further information applicants may contact:

William H. Pitlick, Ph.D.
Health Scientist Administrator
Epilepsy Branch
Neurological Disorders Program
National Institute of Neurological and
Communicative Disorders and Stroke
Federal Building - Room 118
7550 Wisconsin Avenue
Bethesda, Maryland 20205

Telephone: (301) 496-1917

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11/14

NIH GUIDE for GRANTS and CONTRACTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Vol. 11, No. 14, December 31, 1982

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The GUIDE is published at irregular intervals to announce scientific initiatives and to provide policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in grants and contracts activities administered by the National Institutes of Health.

Two types of supplements are published by the respective awarding units. Those printed on yellow paper concern contracts: solicitations of sources and announcement of availability of requests for proposals. Those printed on blue paper concern invitations for grant applications in well-defined scientific areas to accomplish specific program purposes.

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NIH GUIDE FOR GRANTS AND CONTRACTS
Vol. 11, No.14, December 31, 1982

NOTICE

SMALL BUSINESS INNOVATIVE RESEARCH (SBIR) PROGRAM

SMALL BUSINESS INNOVATION DEVELOPMENT ACT OF 1982 (P.L. 97-219)

PUBLIC HEALTH SERVICE

P.L. 97-219, an amendment to the Small Business Act, requires agencies of the Public Health Service (PHS) and certain other federal agencies to set aside a specified amount of their research and development (R&D) budgets for a Small Business Innovative Research (SBIR) Program. This legislation is intended to:

- stimulate technological innovation;
- use small business to meet federal research and development needs;
- increase private sector commercialization of innovations derived from federal research and development; and
- foster and encourage participation by minority and disadvantaged persons in technological innovation.

PHS agencies/offices participating in the SBIR Program include the National Institutes of Health (NIH), the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA), the Centers for Disease Control (CDC), the Food and Drug Administration (FDA), the National Center for Health Services Research (NCHSR), and the Office of Adolescent Pregnancy Programs (OAPP). NIH accounts, however, for approximately 94% of the SBIR set-aside funds in PHS.

For purposes of the SBIR Program, a "small business" is any organization that is independently owned and operated for profit, not dominant in the field in which it is operating and meets the size standard of 500 or fewer employees.

"Research" or "research and development," when used in reference to the missions of the PHS agencies, refers to (a) a systematic study directed toward greater knowledge or understanding relevant to improving human health and well-being; (b) a systematic study directed specifically toward applying new knowledge to meet a recognized health need; or (c) a systematic application of knowledge toward the production of useful materials, devices, and systems or methods, including design, development and improvement of prototypes and new processes to meet specific requirements in the health area.

IMPLEMENTATION OF THE SBIR PROGRAM

The SBIR Program of the PHS will consist of the following three phases:

Phase I: establishing the technical merit and feasibility of R&D ideas which may ultimately lead to commercial products or services in the health area. This phase must precede the submission of Phase II requests for funding.

Phase II: in-depth development of proposed R&D ideas that are likely to result in commercial products or services, with special consideration given to proposals demonstrating prospective private capital commitments for commercial applications.

Phase III: only where appropriate, the involvement of private capital for commercializing the results of R&D funded by a federal agency, or the involvement of non-SBIR funded contracts with a federal agency for products or processes intended for use by the U.S. government.

The Public Health Service (PHS) wishes to identify small businesses that may have the expertise to contribute to the R&D mission of these agencies. Small business firms which believe that they have such capabilities should contact the office indicated below. A solicitation for grant applications will be available shortly which will provide detailed information on implementation of the SBIR Program, grant application and review procedures, and the R&D needs of the agencies which lend themselves to performance by small businesses. SBIR solication for R&D contract proposals relevant to specific agency requirements will be announced at a later date.

Small businesses interested in contracts for R&D support services, as distinct from R&D *per se*, should pursue opportunities through the regular small and small disadvantaged business set-aside programs. PHS agencies will continue to entertain responses to competitive contract solicitations from the small business sector in program areas not covered by SBIR Program Solicitations.

Small Business Conference

The PHS invites the participation of small-business R&D firms in a conference to be held at NIH in early February 1983. The purpose of the conference will be to discuss agency implementation of the SBIR Program and to offer an opportunity for small-business scientists to discuss R&D needs with PHS program staff.

If you are interested in receiving a copy of the Program Solicitation of a given PHS agency and/or attending the Small Business Conference, please contact:

Office of Grants Inquiries
Division of Research Grants
National Institutes of Health
Westwood Building - Room 449
Bethesda, Maryland 20205

NOTICE

SMALL GRANT APPLICATIONS

ALCOHOL, DRUG ABUSE, AND MENTAL HEALTH ADMINISTRATION

The Alcohol, Drug Abuse, and Mental Health Administration urges prospective small grant applicants to give careful attention to the following:

1. Obtain special information and instructions for preparation of the application from the appropriate institute, e.g., National Institute of Mental Health (NIMH), National Institute on Alcohol Abuse and Alcoholism (NIAAA), and National Institute on Drug Abuse (NIDA).
2. Clearly identify the mailing envelope as containing an ADAMHA SMALL GRANT APPLICATION
3. Do not package with other types of applications.
4. Submit the application to the Division of Research Grants (DRG) as early as possible.

Adherence to the above should facilitate prompt processing of the applications.

ERRATUM

NIGMS SHARED INSTRUMENTATION GRANTS

NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

An Announcement in the November 5, 1982, NIH Guide for Grants and Contracts (Vol. 11, No. 12) printed on page 13, from the National Institute of General Medical Sciences, had an error in the Institute's name. The correct name for the Institute is the **NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES.**

NOTICE

INDIVIDUAL NRSA APPLICATION FORMS PHS 416-1 AND PHS 416-9

DIVISION OF RESEARCH GRANTS

The new competing Individual National Research Service Award (NRSA) Application Form (PHS 416-1, revised 12/81 and announced in the NIH Guide for Grants and Contracts, Vol. 11, No. 11, October 8, 1982, is now available. Copies of this form may be obtained by writing to:

Chief, Office Services Section
Division of Research Grants
National Institutes of Health
Bethesda, Maryland 20205

Individual copies may be obtained by writing to:

Office of Grants Inquiries
Division of Research Grants
National Institutes of Health
Bethesda, Maryland 20205

Because of the proximity of the February 1, 1983 deadline, the National Institutes of Health (NIH) will accept the 11/79 revision of Form PHS 416-1 for that deadline. The 12/81 revision should be used exclusively for deadlines after February 1, 1983.

Competing applications mailed out by NIH will include updated information statements describing the Postdoctoral Fellowship (July 1, 1982) or Senior Fellowship (October 1, 1982) as appropriate. Individual copies of these statements are available from the Office of Grants Inquiries at the address identified above.

The noncompeting Individual NRSA Continuation Application Form PHS 416-9, revised 12/81, was put into use in late November. NIH will continue to mail fellowship continuation forms directly to individual fellows at the appropriate time. This form will not be distributed through institutional control offices.

NOTICE

RESEARCH LACKING PLANS FOR INVOLVEMENT OF HUMAN SUBJECTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

On January 26, 1981, the Department of Health and Human Services (DHHS) revised its regulations for the protection of human subjects. 45 CFR 46.118 addresses applications and proposals lacking definite plans for involvement of human subjects.

> Certain types of applications for grants, cooperative agreements, or contracts are submitted to the Department with the knowledge that subjects may be involved within the period of funding, but definite plans would not normally be set forth in the application or proposal. These include activities such as institutional type grants (including bloc grants) where selection of specific projects is the institution's responsibility; research training grants where the activities involving subjects remain to be selected; and projects in which human subjects' involvement will depend upon completion of instruments, prior animal studies, or purification of compounds. These applications need not be reviewed by an IRB before an award may be made. However, except for research described in 46.101(b) (exempted research) no human subjects may be involved in any project supported by these awards until the project has been reviewed and approved by the IRB, as provided in these regulations, and certification submitted to the Department.

In activities such as the above, even though an IRB review need not take place at the time of submission of the application, DHHS requires the attachment to the application of the Form HHS-596, "Protection of Human Subjects Assurance/Certification/Declaration." This form may serve either as a certification that IRB review and approval has taken place for the research proposed in the application, or as a pledge that review and approval and submission of a certification will occur before human subjects are involved in the research.

In many instances trainees supported by institutional training grants will be participating in research supported by research project grants, for which the IRB review of human subjects is already complete. This review is sufficient providing that the research would not be substantially modified by the participation of a trainee.

For proposed projects in which the research has received IRB review and approval, block 5 of the Form HHS-596, "Certification of IRB Review and Declaration of Exemption," should indicate the date of review. For research in which definite plans are not set forth in the application, instead of checking a box in block 5 of the Form HHS-596, the applicant should write "See Note," and on the reverse of the form indicate the following: "This is an institutional research training grant (for example) for which plans are not definite. A certification of IRB review and approval of research involving human subjects will be provided before the activity begins if certification has not already been filed. This is in accord with 45 CFR 46.118."

NOTICE

ALCOHOL RESEARCH GRANTS AND NEW INVESTIGATOR RESEARCH AWARD

PROGRAM ANNOUNCEMENTS NOW AVAILABLE

NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM

Updated program announcements providing current information about areas in which support is available from the National Institute on Alcohol Abuse and Alcoholism (NIAAA) are now available. In addition to the Institute's interest in supporting research on the etiology of alcoholism and the adverse consequences of alcohol abuse, it should be noted that there are several high priority areas in the Alcohol Research Grants program announcement; namely, treatment research, prevention research, and research on alcohol-related accidents, injuries, and violence. Of special interest are treatment and prevention research studies that are focused on high priority groups such as teenagers and women.

Potential applicants for Alcohol Research Grants and for New Investigator Research Awards may obtain these updated program announcements from:

Division of Extramural Research
National Institute on Alcohol Abuse
and Alcoholism
Parklawn Building - Room 14C-17
5600 Fishers Lane
Rockville, Maryland 20857

Applications must be received by March 1, 1983, to be eligible for funding in FY 1983.

NOTICE

PUBLIC BRIEFING MEETINGS BY THE

NATIONAL HEART, LUNG, AND BLOOD ADVISORY COUNCIL

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

The National Heart, Lung, and Blood Advisory Council will hold four public briefing meetings for the purpose of informing biomedical scientists, administrators, volunteer health organizations, and the public about the status of the National Heart, Lung, and Blood Institute (NHLBI) and about possible strategies for achieving and maintaining a balance of program mechanisms and for protecting the number of research grants awarded by the Institute. The briefing meetings are designed as an educational effort that will also provide the opportunity for the Council and the NHLBI to hear directly from those interested in and concerned about the future of the Institute's extramural programs.

The public meetings will be held at the following times and locations:

February 24-25, 1983

WASHINGTON, D.C.
9:00 a.m.
Lister Hill Auditorium, Building 38A
National Institutes of Health

March 3-4, 1983

SAN FRANCISCO, CALIFORNIA
9:00 a.m.
San Francisco Hilton and Tower
333 O'Farrell Street

March 24-25, 1983

NEW ORLEANS, LOUISIANA
9:00 a.m.
International Hotel
300 Canal Street

April 14-15, 1983

CHICAGO, ILLINOIS
9:00 a.m.
Radisson Chicago Hotel
505 North Michigan Avenue

Send requests for a complete statement of the purpose of these meetings to:

Public Briefing Meetings
National Heart, Lung, and Blood
Advisory Council
National Heart, Lung, and Blood Institute
National Institutes of Health
Building 31 - Room 5A-03
Bethesda, Maryland 20205

Those who wish to speak at a briefing meeting must submit a written request to the National Heart, Lung, and Blood Advisory Council no later than January 21, 1983. The request to speak must include the following:

1. The name of the person who wishes to address the Council;
2. The professional affiliation of the requesting speaker, if appropriate;
3. A brief summary of the statement that would be presented; and
4. The address and telephone number where the requesting speaker can be reached during business hours.

Speakers will be selected from the constituencies who look to the Institute to advance knowledge about heart, lung, and blood diseases and from others whose interests correspond to the extramural programs of the NHLBI.

Each speaker will be allowed about ten minutes. A list of speakers for a meeting will be sent in advance to the region in which that particular meeting will be held. Additional written comments of any length may be submitted, at any time, for distribution to the Council. The results of these briefing meetings, including the texts of the speakers and all other materials submitted, will be available in the summer of 1983. For further information, please call (301) 496-6331.

ANNOUNCEMENT

REQUEST FOR RESEARCH GRANT APPLICATIONS:

RFA-NIH-NCI-DRCCA-82-17

PATTERNS OF CARE FOR ELDERLY CANCER PATIENTS:

IMPLICATIONS FOR CANCER CONTROL

NATIONAL CANCER INSTITUTE

Application Receipt Dates: April 19, 1983 and December 6, 1983

I. PURPOSE

The National Cancer Institute (NCI) invites qualified researchers to submit grant applications for research projects to investigate problems and needs unique to the elderly in the diagnosis and management of cancer. NCI, in consultation with the National Institute on Aging (NIA), is directing a specific focus on the older adult who has cancer. Although the majority of cancers affect older persons disproportionately and the probability of developing cancer increases as one grows older, relatively little is known about how the problems of old age affect cancer patient work-up, treatment and care. The dearth of data makes it impossible to provide definitive answers to the many questions which arise about the impact of old age on cancer patient management.

As a cancer control effort for the elderly, NCI is encouraging studies directed toward the interface of cancer and aging. The major objective of cancer control is to reduce cancer incidence, morbidity, and mortality through an orderly sequence from conducting research on interventions and their impact in defined populations to their broad, systematic application to the general population. Research support will be provided under the auspices of NCI's Division of Resources, Centers, and Community Activities (DRCCA). DRCCA's cancer control mandate, authorized by Congress, includes the responsibility to study and bring into medical practice proven research which will improve prevention, detection, diagnosis, and treatment of cancer.

Old people in poor health frequently present a chronic disease complex which is long-term and severely debilitating. When cancer is linked with the chronic disabling conditions which persons acquire over the course of their lives, medical decision-making and differences in management must often be uniquely applied to

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This program is described in the Catalog of Federal Domestic Assistance No. 13.399, Cancer Control. Awards will be made under the authority of the Public Health Service Act, Title IV, Section 403 (Public Law 78-410, as amended; 42 USC 284) and administered under PHS grant policies and Federal regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

the older-aged patients. Decisions are influenced not only by the cancer signs and symptoms with which patients present, but also by their frailty; other health difficulties and chronic disabilities; and social, psychological, and economic handicaps. Advancing age with its concomitant changes in physical ability, physiological function, and social relationships complicate providing care to elderly cancer patients. Physicians must consider these various factors when planning cancer treatment and care recommendations for the elderly. Thus, the assessment of the patterns of care (i.e., the diagnosis, work-up, staging, and treatment) for evaluation of elderly cancer patients requires an adequate data base.

The purpose of this Request for Applications (RFA) is to solicit high quality research grant applications that address the mutual interests and concerns about cancer and old age as they interact and relate to clinical research and medical practice so as to contribute to our understanding of the management of cancer in the elderly. This initiative, by stimulating the fields of oncology, geriatrics, gerontology, and other relevant disciplines and professions to conduct multidisciplinary research, is intended to reduce the knowledge gap about cancer treatment and care in the older-aged population. Information is being sought on the natural history of cancer in the elderly, treatment patterns, the interaction of the normal and/or pathophysiological processes of aging and cancer, the overlap of intercurrent disease with cancer, and the extent to which interdisciplinary approaches may foster coordinated application of special skills for optimal cancer care for the elderly.

II. STATEMENT OF THE PROBLEM

Cancer is primarily a disease which occurs in the older-aged segment of the population. Approximately 50 percent of all cancers occur in persons 65 years and older; close to 60 percent of all cancer deaths occur after 65 years of age. The risk of developing cancer increases rapidly with each decade of life. Incidence data from the Surveillance, Epidemiology, and End Results (SEER) Program of the Biometry Branch, NCI, reveal that the average annual age-specific incidence rate for ages 65-69 years is 1360.6 per 100,000 persons. This is almost double the rate of 748.8 observed for those aged 55-59 years. The 75-79 years of age group reflects a continuing increase to 2028.9 per 100,000 persons with the rise peaking at 2308.0 for those 85 years and older.

Not only does cancer affect the older age group in our society disproportionately, but the nation's number of older persons is gradually increasing and will constitute a larger percentage of the population in the future. In 1900, the over 65 years of age group numbered 3.1 million persons and represented only 4.1% of the entire population. By 1975, this same age group had 22.4 million persons and represented 10% of the population; estimates for the year 2000 predict a rise to 33.2 million persons making up almost 12% of the U.S. population. By 2030, possibly the peak year for the overall growth of the population, there will be approximately 55 million persons 65 years or older in the U.S. Coupled with these increases is the expansion of the 75 and older population segments of the age categories. There are and will be more persons 85 years of age and older. Clearly, within the context of the U.S. health care system, there will be more old people who require cancer care.

In the area of early detection, when the older person enters the medical care system could be significant for the course of potentially malignant lesions. Early detection efforts for older persons have been minimal. There is no information on what older persons do when they become aware of themselves as ill with signs and symptoms of cancer and the factors affecting promptness in their decisions to seek care.

When considering surgical, radiotherapeutic, chemotherapeutic or a combination of these therapies, age-imposed compromises are particularly true for the very young and the elderly. Anatomic development and degeneration as well as physiologic factors must always be considerations in these situations.

The selection of surgical procedures which are conservative or aggressive in approach and palliative or curative in intent will be influenced by age, as will the incidence of complications during the postoperative recovery period. There are limited data relative to the choice of surgical treatment in the elderly.

Administering radiotherapy to the aged cancer patient is a common practice, yet again little information is available related to the incidence and type of complications associated with advancing age. Tolerance to irradiation varies with the radiation fields, dosage, and type of cancer under treatment.

Age-dependent differences in drug absorption, distribution, metabolism, and excretion are all appreciated. Drug-drug interactions receive less attention but represent a significant hazard in the multiple medicated elderly. Adverse drug reactions (e.g., the stomatitis from adriamycin or 5-fluorouracil) in the elderly may represent life-threatening situations. Changes in physiology (e.g., decreased renal function), anatomy (e.g., intracavitary fluid retention acting as a drug reservoir), and rapid weight changes altering drug-to-weight ratios all represent potentially hazardous changes for these patients.

Health professionals should also be able to distinguish between the changes that occur as a result of aging and those which may be attributed to cancer and other disease processes. In addition to having a sound clinical information base and a variety of skills in cancer care and treatment, oncology professionals must be able to carry on surveillance and monitoring for the concomitant effects of aging. In the normal process of aging, significant changes occur in body structure, composition, and function. The skin and mucosa grow thinner, stature decreases as the skeletal frame settles, functional capacities of organs decline, bone mass decreases, muscle size and strength are diminished, sensory loss occurs over time, the systems (e.g., pulmonary, digestive, cardiovascular, renal, nervous, and endocrine) undergo multiple changes which result in a diminution of many important functions. These changes occur over time and most persons accommodate to the changes. But the altered levels of functioning and decreased sensitivities when accompanied by an illness such as cancer create a multitude of treatment and care problems for health care providers.

Health professionals who work in oncology settings are often required to apply different skills and techniques to manage various adverse social, economic, and environmental influences which may dominate management decisions for the aged cancer patient. The elderly, perhaps to a greater degree than younger patients, have certain social needs that impact on their health. Together with the stresses of daily living, such age-related life crises as reduced income, loss of loved ones and family support, and changing living arrangements are all interconnected with the older person's physical condition. A thorough understanding of the elderly cancer patient's life situation in conjunction with his or her medical symptoms and course of illness may provide for a more successful treatment regimen. Quality of life issues are relevant to cancer care for the elderly.

III. PROGRAM PLANNING AND RELEVANCE

In September 1981, responding to the paucity of data available and major deficiencies apparent in our knowledge about cancer and its relationship to old age, NCI and NIA co-sponsored a conference which invited professionals working in both fields of cancer and aging to identify and examine a variety of issues in prevention and treatment of cancer in the elderly to ascertain research needs and make recommendations for programmatic direction. Questions arose as to what intervention techniques are available to offset the unusual or specific problems of elderly cancer patients. Since many unsubstantiated or unsupported assertions exist about cancer in old age, conference discussions centered on laying the groundwork for needed research in cancer and aging at the clinical interface of the two fields.

Building upon the conference recommendations for research, this RFA represents an important step toward fulfillment of the congressional intent of the National Cancer Act and Amendments of 1978. Developing information and resources for health professionals in the use of cancer control interventions are major objectives of the cancer control mission.

This RFA is a cancer control project which comes under the program areas of Treatment, Continuing Care, and Rehabilitation (TCCR) in DRCCA. TCCR programs emphasize (1) cancer control research which develops or tests actions or interventions aimed at specific high risk population groups; (2) participation of community physicians in applying advanced treatment research to cancer patients; (3) improved approaches to pain control; (4) development of effective methods to improve the care of advanced cancer patients and support of their families; (5) rehabilitation; (6) expansion of the cancer care knowledge base of physicians, nurses, and other health professionals; and (7) developing information for reducing the social, economic, and emotional burdens which cancer creates for patients and families.

IV. RESEARCH SCOPE

To be responsive to this RFA, investigations which use descriptive and analytic (e.g., longitudinal, cohort, case-control, and cross-sectional) designs are acceptable. The study population in which the research would be conducted should be well defined within a community or the general population. Use of objective, reliable, and valid measures is essential. Study settings may include nursing homes, hospitals, other health care institutions, the community, and the occupational context.

A single or combination of activities from the broad spectrum of early detection, early diagnosis, pre-treatment evaluation, treatment, rehabilitation, and continuing care cancer control efforts may be addressed. Topics of major interest to DRCCA are listed below. However, grant applications are not limited to these areas. The list is neither all-inclusive nor exclusive, nor is it an order of priority of interest. Related issues designated by the applicant will be considered as well.

- Patterns of care for the elderly cancer patient.

  Not much is known about how physicians care for older-aged cancer patients at the community level. Neither has there been a distinct focus on the behavior of neoplasms and tumor characteristics as they present in the elderly. It is known, however, that multiple clinical problems of the aged frequently require physicians to look for subtle or masked features of adverse conditions in addition to the presenting complaint. These special features of aging and symptoms of illness in old age influence the treatment and care of the elderly cancer patient and tend to complicate carrying out prescribed regimens. Studies are needed on the assessment of the effectiveness of different treatments relative to cancer, the stage of the disease, and significant features and characteristics of old age (e.g., poor repair mechanisms, functional loss, greater susceptibility to toxicity of treatment). In these types of studies, a special effort should be made to minimize biases, for example, through the use of defined populations.

- Variations in response factors to signs and symptoms of cancer by older aged persons.

  To a large extent, improved cancer cures depend on early recognition and appreciation of signs and symptoms of the disease and prompt referral to treatment. The actions taken by older persons in response to the signs and symptoms of cancer will affect the cure, number of complications, and sequelae. Elderly persons are often directly or indirectly excluded from most early cancer detection efforts. Though they represent one of the groups at highest risk, older aged persons have not been singled out as a target group. Research strategies toascertain what factors influence decisions made by older persons in response to signs and symptoms of cancer and the individual variations which may result in delay are needed.

- Analysis of existing data bases which are relevant to addressing cancer patient management for older aged persons.

  Secondary analyses of surveys or studies which have been designed to address other issues in treatment of cancer or other chronic illnesses, the processes of normal aging, long-term care, and related health issues may be appropriate. This choice would require a thorough and detailed explanation of the data elements in the data base identified as a candidate for this research to determine the utility of addressing the problems at the interface of cancer and aging raised in this RFA. Special attention must be given to ascertaining biases in the data base.

- Evaluation of tolerance of and response to standard or experimental chemotherapy regimens.

  Studies should involve entry of patients across the entire age spectrum (with efforts to minimize selection bias) into predetermined chemotherapy protocols with doses based either on surface area or adjusted for physiologic parameters such as creatinine clearance. Data should be collected on other factors known to affect toxicity or response to therapy so that the independent effect of age can be evaluated in a multivariate model. Tumors selected for study should be those of intermediate sensitivity to chemotherapy such as breast cancer, small cell lung cancer, head and neck cancer and ovarian cancer so that one has a reasonable statistical probability of observing either increases or decreases in response rate as an effect of age. A similar approach might be considered for surgery, radiation therapy, or multimodality treatment interventions.

- Socio-emotional and economic consequences of cancer for the older person and family members.

  Cancer is an isolating illness, and old age is an isolating phenomenon. As a person grows older, various forms of social support diminish. There is a decline in social network involvement. Geographic distance may preclude kinship network involvement. The older individual may experience loss of friends, family, and spouse. Sickness may also be demoralizing and alienating. Often the cancer patient must be cared for in the home by a family member, friend, or spouse who is also in relatively poor health. Then, too, since cancer affects both the patient and family as a unit, family stress, health, and the organization of health behavior are high priorities which may be addressed.

- Epidemiologic Studies.

  Specific questions which address the problems concomitant with old age (e.g., effects of previous illnesses and concurrent illnesses; stages of disease at detection; second primaries; recurrence) in combination with the general epidemiologic concerns about the patterns of disease occurrence and the influential factors are of interest. Much useful information can be derived from epidemiologic studies on incidence and mortality in old age. Experimental epidemiologic approaches (i.e., clinical trials or community trials) to examine treatment, intervention, or preventive efficacy are appropriate.

V. DEFINITION OF "OLD AGE" OR "ELDERLY"

Frequently, old age or elderly is defined using the chronological age of 65 as a point of demarcation. However, this arbitrary age cutoff, while perhaps useful for dealing with age limitations for entitlements or eligibilities for various programs, may not be useful for the research encouraged by this RFA. Applicants should address critically the issue that physiological and chronological ages do not necessarily coincide. With advancing chronological age, there are greater variations in physiological age.

Methods should be proposed by the applicant which express physiological age of the study subjects. For the most part, persons in their middle to late seventies, that is, the older elderly, present the most profound medical problems. Parameters to be considered in describing the elderly patient could include level of physical activity, response to graded levels of physical activity, response to graded levels of exercise, or, in the case of clinical research, measurement of organ function such as creatinine clearance of hepatic clearance of a marker substance.

Thus, the definition of "old age" or "elderly" is flexible for the RFA and is dependent on investigator-defined parameters. Applicants are expected to identify what is meant by "old" in the context of the research and be able to evaluate the correlation of outcome variables and chronological and physiological age.

VI. MECHANISM OF SUPPORT

Applicants funded under this RFA will be supported through the customary National Institutes of Health (NIH) grant assistance award in accordance with Public Health Service (PHS) policies applicable to research project grants including cost sharing. Assistance awards are provided to non-profit organizations and institutions, governments and their agencies, for-profit organiations, and occasionally to individuals when deemed by the PHS to be consistent with legislative intent and program purposes. NCI plans to support up to six awards within the limits of the funds for both review cycles under this RFA if sufficient high quality applications are received. Awards will be for three year projects. Receipt dates for applications are April 19, 1983 and December 6, 1983.

VII. REVIEW PROCEDURES AND CRITERIA

A. Review Panel

Applications responsive to this RFA will be reviewed by an appropriate peer review panel set up by the Division of Extramural Activities (DEA), NCI, NIH. Final review is provided by the National Cancer Advisory Board.

B. Review Criteria

Peer review will consider the following criteria:

1. Relevance and significance of the issues to the overall objectives of the RFA;

2. Scientific merit of the research project design and feasibility of the procedures that are to be used;

3. Potential for evaluating success of the project;

4. Experience, commitment, and leadership ability of the staffing for the research project which must include medical professionals in oncology and/or geriatrics at the leadership level; the qualifications and experience of other members of the study team to do the proposed research;

5. Availability of multidisciplinary expertise from related fields of gerontology, epidemiology, behavioral and social sciences, and health care as required;

6. Adequacy of existing and proposed facilities and resources;

7. Reasonableness of the budget in relation to the research and/or demonstration effort.

8. Adequacy of the proposed means for protecting against hazardous or unethical research procedures.

VIII. METHOD OF APPLYING

Applications should be submitted on the standard research grant application form PHS 398 (Rev. 5/80). Application kits are available at most institutional business offices or from the Division of Research Grants (DRG), NIH.

A. Letter of Intent

1. Applicants are encouraged to submit a letter of intent addressing the following topics:

   a. A brief description of the intended project.

   b. A description of available research facilities.

   c. Positions and research interests of the principal investigator(s) and staff who will be involved in the study.

   d. Plans for oncology and geriatric medical collaboration, delineation of staff roles, manner of anticipated participation of principal investigator(s) and multidisciplinary approach.

   e. Projections for patient involvement in the study.

B. Timetable

Letters of Intent	Receipt of Applications	NCAB Review	Earliest Possible Award Date
Feb. 15, 1983	Apr. 19, 1983	Oct. 3-5, 1983	Dec. 1, 1983
Sept. 15, 1983	Dec. 6, 1983	May 16-18, 1984	July 1, 1984

C. Consequences of Lack of Responsiveness to the RFA or Late Submission

Based upon the letter of intent, potential applicants will be promptly advised whether or not their proposal is found to be within the research goals and scope of the program as defined in this RFA. Grant applications that are not responsive to the RFA or are not received on or before April 19, 1983, will not be accepted for review in the first cycle. They will be deferred to the second review cycle. Applications not received on or before the second receipt date of December 6, 1983, will be returned to the applicant.

D. Format for Applications

The conventional presentation for grant applications should be utilized. The points identified under the Review Criteria must be considered. The words "RFA: PATTERNS OF CARE FOR ELDERLY CANCER PATIENTS: IMPLICATIONS FOR CANCER CONTROL" must be typed in bold letters in line number 2 of the face page of the application.

Please enclose a cover letter indicating that the application is in response to this RFA. A copy of the cover letter should also be sent to Dr. Rosemary Yancik, NCI, DRCCA, at the address provided.

E. Application Procedure

Applications must be received on or before the application receipt dates stipulated above. The original and six copies of the application should be sent or delivered to:

Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205

Two additional copies should be sent to:

Referral Officer, Grants Review Branch
Division of Extramural Affairs
National Cancer Institute
National Institutes of Health
Westwood Building - Room 826
5333 Westbard Avenue
Bethesda, Maryland 20205

F. Inquiries and Correspondence

All correspondence related directly to application development, letters of intent, and the copies of the cover letter which accompany the applications should be directed to:

Rosemary Yancik, Ph.D.
Division of Resources, Centers, and
  Community Activities
National Cancer Institute
Blair Building - Room 729
Bethesda, Maryland 20205

Telephone: (301) 427-8636

Questions pertaining to business matters should be addressed to:

Mr. William G. Wells
Grants Management Specialist
Grants Administration Branch, OD
National Cancer Institute
National Institutes of Health
Westwood Building - Room 852
Bethesda, Maryland 20205

Telephone: (301) 496-7444

ANNOUNCEMENT

SMOKELESS TOBACCO AND NON-TOBACCO SMOKING PRODUCT USE:*
IDENTIFICATION OF INITIATION MECHANISMS IN CHILDREN AND ADOLESCENTS

DIVISION OF RESOURCES, CENTERS AND COMMUNITY ACTIVITIES

NATIONAL CANCER INSTITUTE

The Division of Resources, Centers, and Community Activities (DRCCA) of the National Cancer Institute (NCI) has the principal Federal responsibility for assuring the rapid and effective application of cancer research findings in the fields of prevention, detection, diagnosis, treatment, rehabilitation, and continuing care. DRCCA's goal is to develop the means for reducing cancer morbidity and mortality.

As part of its responsibilities in the area of cancer prevention, DRCCA is expanding its program initiatives under the NCI's Smoking, Cancer and Health Program ** which has been designed to facilitate the development of effective approaches to smoking prevention and cessation. The purpose of this Announcement is to encourage research activities which will: (1) identify factors that lead to the use of smokeless tobacco and/or non-tobacco smoking products (NTSP) by children and adolescents; (2) identify those conditions which may lead to shifts in tobacco usage patterns; and (3) develop prevention and cessation strategies which can be integrated into school based health and/or anti-smoking programs.

I. RATIONALE

Shifts in tobacco usage patterns and initiation of non-tobacco smoking behaviors have been reported by the research community. Data published by the USDA indicate that 11 million Americans use smokeless tobacco annually.[1] This figure represents a 12% annual increase in smokeless tobacco use since 1974.[1] In addition, the recent introduction of NTSP increases the potential for recruitment to smoker behavior by offering alternate smoking products.

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* For purposes of this Announcement smokeless tobacco is defined as chewing, dipping, or snuffing commercial tobacco products; non-tobacco smoking products are defined as commercially sold "smokes."

** NIH Guide for Grants and Contracts Vo. 9, No. 1, January 3, 1980.

[1] Smoking & Health, A Report of the Surgeon General DHEW Publication No. (PHS) 79-50066.

This program is described in the Catalog of Federal Domestic Assistance No. 13.393, Cancer Cause and Prevention. Awards will be made under the authority of the Public Health Service Act Section 301(c) and Section 402, PL 78-410, as amended; (42 USC 241 and 282) and administered under PHS Grant Policies and Federal regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

Epidemiological evidence suggests that use of smokeless tobacco increases the risk of oral cancer.[2] While little scientific evidence is available on NTSP, preliminary reports suggest that constituents in the gas phase of the smoke are suspected contributors to impairment of lung functioning, as well as acting as potential promoters of neoplastic disease.[3] In addition, multiple tobacco use, (e.g., dipping and smoking) is a likely contributor to an increased cancer risk.

II. RESEARCH GOALS AND SCOPE

These projects should focus on the development of research strategies to identify, within well-defined population group(s)--e.g., junior high school students--the antecedents and correlates associated with initiation of smokeless tobacco and/or non-tobacco smoking product use and identification of those concurrent or interacting conditions which may lead to shifts from these products to regular tobacco cigarette smoking. Evaluation of possible changes in knowledge, attitudes, beliefs, and behavior concerning the use of non-traditional smoking and smokeless tobacco products and/or the decision to shift from these products to regular tobacco cigarette smoking will be considered a major component of the research design. Due to the generally similar behavior correlates between use of these products and cigarette smoking, demonstrated knowledge of the relevance and significance of current smoking prevention and cessation strategies aimed at children and adolescents is to be included in the research design. Knowledge of the psychological and social mechanisms potentially inherent in recruitment to these products is a general requirement. In addition, the investigators must demonstrate as in depth knowledge of state-of-the art research in the areas of smokeless tobacco and NTSP as well as regular tobacco cigarette smoking as it relates to the research population. In addition to self-report, the study design should include biochemical measurements to increase the validity of self-reports, as well as to provide independent estimates of levels of tobacco use.

Description of the research populations, rationale for the method of sampling, definition of the variables and size of the group, as well as proven access and cooperation from intended research population, school authorities, parents will be required.

This program is, therefore, seeking grant applications concerned with basic and applied studies in prevention of disease with emphasis on behavioral, cognitive, attitudinal and motivational factors, as well as other appropriate research areas.

III. GENERAL INFORMATION

It should be emphasized that this statement of interest in developing new grant applications is neither a Request for Applications (RFA-Grants) nor a Request for Proposals (RFP-Contracts), but rather an announcement of the NCI's intent to stimulate investigator-initiated research in the stated area. As such, proposals are reviewed by the usual National Institutes of Health (NIH) peer review groups for technical merit and recommendation to the National Cancer Advisory Board.

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[2] Christen, A.G., Armstrong, W.R., McDaniel, R.K., "Intraoral Leukoplakia, Abrasion, Periodontal Breakdown and Tooth loss in a Snuff Dipper," JADA, Vol. 98, April 1979.

[3] Personal Communication from Oak Ridge National Laboratories to NCI, 10-23-80.

Additional needs for specific, in-depth activity in any or all of the Programs may be met in the future with issuance of RFAs and/or RFPs.

The announcement leaves the choice of specific research objective, identification of specific aims, development of appropriate protocols and methodology, and the procedures of analysis and interpretation of data to the investigators' initiative. However, once the award is made under the program, any substantial modification of the research originally proposed must be mutually agreed upon by the investigator and the respective NCI division.

For purposes of tracing responses to this program announcement, investigators should indicate its title on line 2, page 1 of the PHS 398 grant application.

IV. APPLICATION AND REVIEW PROCEDURES

A letter of intent and requests for additional information should be sent to:

Catherine S. Bell, M.S.
Program Director for Behavioral Smoking Projects
National Cancer Institute (DRCCA) (BMB)
Blair Building - Room 629
8300 Colesville Road
Bethesda, Maryland 20205

Telephone: (301) 427-8656

Application kits may be obtained from an organization's application control office or from the:

Division of Research Grants
National Institutes of Health
Bethesda, Maryland 20205

The application receipt dates for grants submitted under this program announcement are those indicated in PHS form 398.

Completed applications are to be sent to:

Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205

ANNOUNCEMENT

TOBACCO AND THE BLUE COLLAR WORKER

DIVISION OF RESOURCES, CENTERS AND COMMUNITY ACTIVITIES

NATIONAL CANCER INSTITUTE

The Division of Resources, Centers, and Community Activities (DRCCA) of the National Cancer Institute (NCI) has the principal Federal responsibility for assuring the rapid and effective application of cancer research findings in the fields of prevention, detection, diagnosis, treatment, rehabilitation, and continuing care. DRCCA's goal is to develop the means for reducing cancer morbidity and mortality.

As part of its responsibilities in the area of cancer prevention, DRCCA is expanding its program initiatives under the NCI's Smoking, Cancer and Health Program* which has been designed to facilitate the development of effective approaches to smoking prevention and cessation. The purpose of this announcement is to encourage research activities which will: (1) identify those factors that lead to recruitment, maintenance, cessation, and recidivism as related to tobacco use in the blue collar population; (2) identify concurrent and interacting conditions which may lead to shifts in tobacco usage patterns; and (3) develop prevention and cessation strategies which can be integrated into planned or on-going workplace based health/and or anti-smoking programs.

I. RATIONALE

This program announcement was developed in response to survey research data which indicate that 51% of the blue collar workers are smokers as contrasted with 37% of the total smokers in the U.S. population. In addition, research data suggest that blue collar workers have a potentially greater risk of exposure to known and suspected carcinogenic substances in the workplace. This occupational exposure may act in synergy with smoking behavior thus exacerbating the risk of cancer for this population.[1]

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*NIH Guide for Grants and Contracts Vol. 9, No. 1, Janurary 3, 1980.

This program is described in the Catalog of Federal Domestic Assistance No. 13.393, Cancer Cause and Prevention. Awards will be made under the authority of the PHS Act Section 301(c) and Section 402, PL 78-410, as amended; (42 USC 241 and 242) and administered under PHS Grant Policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

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[1] Surgeon General's Report on Health Consequences of Smoking 1979.

II. RESEARCH GOALS AND SCOPE

These projects will focus on the development of research strategies to identify, within a well-defined population group(s)--e.g., asbestos workers, who are tobacco users--the antecedents, correlates and consequences that are related to recruitment, maintenance, recidivism, and cessation of tobacco use in blue collar workers. The study design should include identification of those concurrent and interacting conditions which may lead to shifts in tobacco usage patterns--e.g., from non-user to user, occasional user to regular user, regular user to non-user, cigarette smoker to smokeless tobacco user, etc. The project should focus on the individual, social, and environmental factors that determine the influences affecting tobacco use in the blue collar worker, e.g., occupational related stress. social support and interaction effects, need for stimulation, maintenance of status, etc. Knowledge of the adverse health effects that result from the interaction between tobacco use and exposure to known and suspected carcinogens in the workplace will be a general requirement. The study design should include a reliable definition of the status of tobacco usage among blue collar workers and should consider multiple forms of tobacco use, e.g., regular tobacco cigarettes, cigars and pipes, non-tobacco smoking products, chewing, and dipping. In addition to self-report, the study design should include biochemical measurements to validate self-reporting, as well as to provide independent estimates of levels of tobacco use. The investigator should address application of research results to future prevention and cessation strategies.

Description of the research population, rationale for the method of sampling, definition of the variables and size of the sample, as well as proven access and cooperation from the intended research sample and appropriate labor and management representatives will be required.

The program is, therefore, seeking grant applications concerned with basic and applied studies in disease prevention with an emphasis on behavioral, attitudinal, and motivational factors, as well as other appropriate research areas.

III. GENERAL INFORMATION

It should be emphasized that this statement of interest in developing new grant applications is neither a Request for Applications (RFA - Grants) nor a Request for Proposals (RFP - Contracts), but rather an announcement of the National Cancer Institute's intent to stimulate investigator initiated reserch in the stated area. As such, proposals are reviewd by the usual NIH peer review groups for technical merit and recommendation to the National Cancer Advisory Board. Additional needs for specific, in-depth activity in any or all of the Programs may be met in the future with the issuance of RFAs and/or RFPs.

The announcement leaves the choice of specific research objective, identification of specific aims, development of appropriate protocols and methodology, and the procedures for analysis and interpretation of data to the investigators' initiative. However, once the award is made under the program, any substantial modification of the research originally proposed must be mustally agreed upon by the investigator and the respective NCI division.

For purposes of tracing responses to this program announcement, investigators should indicate its title on line 2, page 1 of the PHS 398 grant application.

IV. APPLICATION AND REVIEW PROCEDURES

A letter of intent is encouraged and requests for additional information should be sent to:

Catherine S. Bell, M.S.
Program Director for Behavioral Smoking Projects
National Cancer Institute, DRCCA, BMB
Blair Building - Room 629
8300 Colesville Road
Bethesda, Maryland 20205

Telephone: (301) 427-8656

Application kits may be obtained from an organization's application control office or from the:

Division of Research Grants
National Institutes of Health
Bethesda, Maryland 20205

The application receipt dates for grants submitted under this program announcement are included in PHS form 398.

Completed applications are to be sent to:

Division of Research Grants
Westwood Building - Room 240
National Institutes of Health
5333 Westbard Avenue
Bethesda, Maryland 20205

ANNOUNCEMENT

NEW NIH BIOTECHNOLOGY HIGH VOLTAGE ELECTRON MICROSCOPE (HVEM)

RESOURCE AVAILABLE TO BIOLOGICAL AND MEDICAL RESEARCHERS

DIVISION OF RESEARCH RESOURCES

The Biotechnology Resources Program (BRP), Division of Research Resources (DRR), National Institutes of Health (NIH), is supporting part of the operation of the 1.2 million volt electron microscope at the Albany, New York State Department of Health installation, under the direction of Dr. Donald Parsons, to provide access to national users.

This installation is operated as a State facility in the Northeast Region, and is now available on a national basis to users, who are qualified scientists with appropriate biomedical projects, irrespective of institutional affiliation or geographical location.

In applying, the need for, or appropriateness of the Albany installation should be stated. Interested scientists should submit a brief proposal (one to four pages) which includes the following information:

1. Title, name, address and phone number.
2. Curriculum vitae of the investigator.
3. Description of the proposed project, of which the HVEM study will be a part.
4. Statement of the biomedical value of the project.
5. Justification for the use of the HVEM; explanation of its appropriateness to the project proposed.
6. Results already obtained by light or conventional electron microscopy at 100 KV, 200 KV or lower voltages. Selected micrographs should be enclosed.
7. Nature of the specimens, specific methods used in specimen preparation and suitability for HVEM should be documented.
8. A concise bibliography directed relevant to the proposed project should be given.
9. An initial visit for a pilot study will be allowed in relation to your plan for microscope time, which must be estimated in your application. Further visits will be subject to review by the Advisory Committee.

Potential users are encouraged to consult members of the Resource Group, and the Advisory Committee, for technical advice on specimen preparation and advance study advisable before a visit. Instructions on HVEM technique and the various modes of operation and the accessories of the HVEM are available from the Resource and should be obtained early. Periodic workshops on the theory and practice of HVEM and associated image processing will be arranged.

Mail your outline to:

Dr. Donald F. Parsons, Director
HVEM Laboratory
Center for Laboratories and Research
New York State Department of Health
Empire State Plaza
Albany, New York 12201

Telephone: (518) 474-7047 or 474-7049

Advisory Committee:

Dr. Lee D. Peachey (Chairman), 217 Leidy Laboratories of Biology G7, University of Pennsylvania, Philadelphia, PA 19104 - Tel: (215) 243-5788.
Dr. Caroline Damsky, Wistar Institute, Philadelphia, PA.
Dr. Barry S. Eckert, State University of New York at Buffalo, Buffalo, NY.
Dr. Robert M. Fisher, US Steel Research Lab., Monroeville, PA.
Dr. Stephen Hui, Roswell Park Memorial Hospital, Buffalo, NY.
Dr. Gordon Kaye, Albany Medical College, Albany, NY.
Dr. William Massover, New Jersey Medical School, Newark, NJ.
Dr. Jean-Paul Revel, California Institute of Technology, Pasadena, CA.
Dr. Sam McGee-Russell, State University of New York, Albany, NY.
Dr. John Wolosewick, University of Illinois Medical Center, Chicago, IL 60612.

ANNOUNCEMENT

AVAILABILITY OF SENIOR INTERNATIONAL FELLOWSHIPS FOR 1984-85

JOHN E. FOGARTY INTERNATIONAL CENTER FOR ADVANCED STUDY IN THE HEALTH SCIENCES

The John E. Fogarty International Center for Advanced Study in the Health Sciences (FIC) announces the availability of senior postdoctoral research fellowships to U.S. health scientists who wish to conduct collaborative research abroad. The purpose of these fellowships is to enhance the exchange of ideas and information in the biomedical, behavioral and health sciences. The types of activity that are supported by this program include collaboration in health sciences, basic or clinical research, and the familiarization with or utilization of special techniques and equipment not otherwise available to the applicant. This program does not provide support for brief observational visits, attendance at scientific meetings, attendance in formal training courses, independent research projects, or full-time clinical, technical or teaching services.

I. ELIGIBILITY REQUIREMENTS

Applicants must meet the following requirements:

1. Be a U.S. citizen or permanent U.S. resident;
2. Hold a doctoral degree in one of the biomedical, behavioral or health sciences;
3. Have five years or more postdoctoral experience;
4. Have professional experience in one of the health, biomedical or behavioral sciences for at least two of the last four years;
5. Hold a full-time appointment on the staff of the U.S. nominating institution;
6. Be nominated by the dean or appropriate U.S. institutional official;
7. Be invited by the foreign institution.

II. APPLICATION AND SELECTION

Fellowship applications are reviewed once annually. The receipt date for Senior International Fellowship applications is June 1, 1983. All applications are reviewed for scientific merit by the National Institutes of Health (NIH). Fellowship awards are made for periods of three to twelve months. A fellowship can be activated within one year after receiving the Notice of Award and the starting date of the fellowship is set by mutual agreement between the fellow and the collaborator at the foreign host institution. Prospective applicants for the Senior International

Fellowship Program may obtain information brochures from FIC. Fellowship applications will be available from the FIC between January 15 and May 15, 1983, and may be requested only by the dean or equivalent institutional official. Information an fellowship applications are available from:

Senior International Fellowship Program
International Research and Awards Branch
Fogarty International Center
National Institutes of Health
Bethesda, Maryland 20205

For an expeditious reply, please send a self-addressed label with your request to the above address.

ANNOUNCEMENT

AVAILABILITY OF SENIOR INTERNATIONAL FELLOWSHIPS FOR 1984-85

JOHN E. FOGARTY INTERNATIONAL CENTER FOR ADVANCED STUDY IN THE HEALTH SCIENCES

The John E. Fogarty International Center for Advanced Study in the Health Sciences (FIC) announces the availability of senior postdoctoral research fellowships to U.S. health scientists who wish to conduct collaborative research abroad. The purpose of these fellowships is to enhance the exchange of ideas and information in the biomedical, behavioral and health sciences. The types of activity that are supported by this program include collaboration in health sciences, basic or clinical research, and the familiarization with or utilization of special techniques and equipment not otherwise available to the applicant. This program does not provide support for brief observational visits, attendance at scientific meetings, attendance in formal training courses, independent research projects, or full-time clinical, technical or teaching services.

I. ELIGIBILITY REQUIREMENTS

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1. Be a U.S. citizen or permanent U.S. resident;
2. Hold a doctoral degree in one of the biomedical, behavioral or health sciences;
3. Have five years or more postdoctoral experience;
4. Have professional experience in one of the health, biomedical or behavioral sciences for at least two of the last four years;
5. Hold a full-time appointment on the staff of the U.S. nominating institution;
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International Research and Awards Branch
Fogarty International Center
National Institutes of Health
Bethesda, Maryland 20205

For an expeditious reply, please send a self-addressed label with your request to the above address.

ANNOUNCEMENT

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

RFA-NIH-NHLBI-DHVD 83G-A

CORONARY ARTERY REACTIVITY, INJURY AND THROMBOSIS

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Application Receipt Date: April 15, 1983

I. PURPOSE

The Division of Heart and Vascular Diseases (DHVD), National Heart, Lung, and Blood Institute (NHLBI), invites grant applications for support of research on the interaction of vascular reactivity, injury, and thrombosis in coronary arteries as contributing factors to myocardial ischemia. Applications received in response to this request will participate in a single competition.

II. DISCIPLINES AND EXPERTISE

Among the disciplines and expertise that may be appropriate for this research are biochemistry, coronary physiology, electrophysiology, hematology and coagulation, hemorrheology, pathology, pharmacology and immunology.

III. BACKGROUND

A. Administrative Background

In 1971, the Institute began a research program of investigation of the fundamental physiology and biochemistry of ischemic myocardium. The program was expanded in 1975, to include research involving the application of laboratory findings to the clinical setting. Subsequently, as the concept of salvageable myocardium developed, emphasis shifted to investigations of interventions which might limit the size of an evolving infarction.

In addition to these research programs, the NHLBI is conducting a clinical trial, The Multicenter Investigation of the Limitation of Infarct Size (MILIS), to assess the efficacy of two drugs, propranolol and hyaluronidase, in limiting the size of an infarct when administered within 18 hours of the onset of symptoms of presumed myocardial infarction. The NHLBI has also supported a substantial number of laboratory and clinical investigations concerning the

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This program is described in the Catalog of Federal Domestic Assistance No. 13.837, Heart and Vascular Diseases. Awards will be made under the authority of the Public Health Service Act, Section 301 (42 USC 241) and administered under PHS grant policies and Federal regulations, most specifically 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

should request travel funds for a two-day meeting each year, most likely to be held in Bethesda, Maryland. Applicants should also include a statement in their applications indicating their willingness to participate in such meetings.

Applicants, who will plan and execute their own research programs, are requested to furnish their own estimates of the time required to achieve the objectives of the proposed research project; however, the award period for this activity will not exceed three years. At the end of the initial award period renewal applications may be submitted for competitive review through the regular grant program of the NIH. It is anticipated that support for this program will begin on September 30, 1983.

The current policies and requirements that govern the research grant programs of the NIH will prevail.

VII. REVIEW PROCEDURES AND CRITERIA

A. Review Method

Applications responding to this RFA will be reviewed for scientific and technical merit by an initial review group, which will be convened by the Division of Extramural Affairs (DEA), NHLBI, solely to review these applications. Upon receipt, applications will be reviewed for their responsiveness to the objectives of this RFA. If an application is judged unresponsive, the applicant will be contacted and given an opportunity to withdraw the application or to have it considered for the regular research grant program of the NIH. If a proposal submitted in response to this RFA is identical to a research grant application already submitted to the NIH for review,the applicant will be asked to withdraw the pending application before the new one is accepted. Simultaneous submission of identical applications will not be allowed.

B. Review Criteria

The factors to be considered in the evaluation of scientific merit of each application will be similar to those used in the review of traditional research-project grant applications; the novelty, originality, and feasibility of the approach; the training, experience, and research competence of the investigator(s); the adequacy of the experimental design; the suitability of the facilities; and the appropriateness of the requested budget to the work proposed. An additional criterion will be the importance of the proposed research to the objectives of this RFA.

VIII. METHOD OF APPLYING

A. Letter of Intent

Prospective applicants are encouraged to submit to the Review Branch of the Institute a one-page letter of intent that includes a brief synopsis of the proposed research and identification of any other participating institutions. The Institute requests such letters for the the purpose of providing an indication of the number and scope of applications to be received. A letter of intent is not binding, and it will not enter into the review of any application subsequently submitted, nor is it a necessary requirement for application.

formation and/or the metabolic products of the thrombus. Conversely it is not known whether vasospasm could induce thrombus formation in the coronary arteries.

Thus it seems timely to encourage fundamental studies of the problem.

IV. OBJECTIVES AND SCOPE

This special grant program is intended to encourage the development of a comprehensive and integrated understanding of the biology and/or pathophysiology of the coronary arteries, particularly in relation to the interplay of factors affecting vasomotion and thrombus formation. These studies may, but not necessarily should, involve an *in vivo* and an *in vitro* component to allow comparison of findings in the same preparation. The peripheral blood vessels may be studied, but only to the extent that the hypothesis and experimental results are relevant to the native coronary circulation. A variety of animal species may be investigated but the model selected should be clearly justified. Human material obtained at surgery or autopsy may also be suitable for these investigations. Topics of interest include, but are not limited to, changes in rheology, the role of formed elements of the blood in, for example, clotting and the production of arachidonic acid metabolites, the role of the various components of the vessel wall, the effect of atherosclerosis on vasospasm, the effects of vasoactive peptides and more generally other neurohormonal factors, and the distribution and density of receptors affecting vascular tone. Also of interest are changes in the mechanical properties of vessel walls and the concomitant changes in collagen and elastin content, which might result in, or be the cause of vasospasm in the coronary arteries.

V. EXCLUSIONS

Studies of the causes of, or factors leading to, progressive atherosclerosis would not be considered responsive to this RFA, unless related to the phenomenon of coronary vasospasm or coronary thrombosis in terms of special conditions pertaining to the specific properties of coronary arteries. Furthermore, studies of injury to heart muscle are not appropriate for this program. Although the research topic may be multidisciplinary, it is not the intent of this request to solicit proposals for large studies encompassing a variety of essentially independent research projects (program projects).

VI. MECHANISM OF SUPPORT

The support mechanism for this program will be the traditional, individual, research-project grant. Although $800,000, total costs, for this program are included in the financial plans for fiscal year 1983, award of grants pursuant to this RFA is contingent upon receipt of funds for this purpose. It is anticipated that six to eight grants will be awarded under this program. The specific amount to be funded will, however, depend on the merit and scope of the applications received and the availability of funds. Since a variety of approaches would represent valid responses to this announcement, it is anticipated that there will be a range of costs among individual grants awarded.

Upon initiation of the program, the DHVD will sponsor periodic meetings to encourage exchange of information among investigators who participate in this program. In the preparation of the budget for the grant application, applicants pathophysiology of myocardial ischemia and therapeutics aimed at limiting infarct size through the Ischemic Heart Disease Specialized Centers of Research (SCOR) Program.

However, these programs are not directed specifically toward elucidating the role of coronary vasomotion and thrombosis in the development of ischemia or the possible effects these two phenomena may have upon each other in causing or exacerbating ischemia and coronary occlusion. Furthermore, while considerable research has been directed toward the injury process in cardiac muscle, little attention has been paid to the occurrence and significance of injury in coronary arteries as a cause or effect of vasospasm and/or thrombosis.

B. Scientific Background

There are two important clinical phenomena which require further research in terms of their significance in ischemic heart disease. (1) Increased tone of large coronary arteries sufficient to cause coronary spasm has been implicated in some cases of clinical myocardial infarction and in a substantial number of patients with rest angina. (2) The occurrence of occlusive thrombi in the coronary arteries has been observed by pathological examination in approximately 80 percent of patients dying of acute transmural myocardial infarction. In addition, occlusion of the infarct-related artery has been documented by coronary angiography in approximately 80 percent of the patients studied in the early hours after infarction. Approximately 75 percent of these completely occluded coronary arteries open with intracoronary thrombolytic therapy to reveal a high grade coronary lesion. This indicates that thrombosis is important in the genesis of myocardial infarction.

Clinical investigators are currently assessing the efficacy of calcium antagonists for the treatment of coronary artery spasm and of thrombolytic agents for the restoration of blood flow in coronary arteries with occlusive thrombi. However, it is clear that these therapies are not necessarily definitive and certainly not curative. For example, recurrent ischemia and/or reocclusion occur in a significant number of patients and it is likely that the underlying lesions, or interplay of precipitating factors remain essentially unchanged. Furthermore, the factors which promote the conversion of a functionally impaired artery, or a marginally functional artery, to one which results in critical coronary spasm and/or thrombosis leading to irreversible myocardial damage are poorly understood. Some evidence suggests that occlusion of an artery reoccurs at a specific location and that there may be special physical, biochemical or anatomic conditions pertaining to that location which predispose it to occlusion. There is also the possibility that varying conditions may exist in the affected location resulting in a cyclic or periodic exacerbation of the ischemia.

A number of mechanisms may be postulated to contribute to coronary spasm, but very little information is available about their relative importance. For example, it is not known to what extent the segment of the coronary artery which undergoes spasm is damaged or contains a non-occlusive thrombus. Although considerable information is available about thrombus formation per se, it is unclear to what extent vasospasm can be induced by thrombus

This letter should be received no later than February 15, 1983, and sent to:

Dr. Charles L. Turbyfill
National Heart, Lung, and Blood Institute
Westwood Building - Room 553
Bethesda, Maryland 20205

B. Format for Application

Submit applications on form PHS 398, the application form for the traditional research-project grant. This form is available in an applicant institution's office of sponsored research or business office orfrom the Division of Research Grants (DRG). Use the conventional format for research-project grant applications and ensure that the points identified in the Section on "Review Procedures and Criteria" are fulfilled.

To identify the application as a response to this RFA, check "yes" on Item 2 of page 1 of the application and enter the title CORONARY ARTERY REACTIVITY, INJURY AND THOROMBOSIS and the RFA number NIH NHLBI-DHVD-83G-A.

C. Application Procedure

Send or deliver the completed application and six (6) signed, exact photocopies of it to:

Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
Bethesda, Maryland 20205

Send an additional twenty (20) copies of the application to:

Review Branch, DEA
National Heart, Lung, and Blood Institute
National Institutes of Health
Westwood Building - Room 5A15
Bethesda, Maryland 20205

Applications must be received by April 15, 1983. An application not received by this date will be considered ineligible, but after discussion with the applicant, it may be considered as a regular research-project grant application.

D. Timetable

Letter of intent	February 15, 1983
Application receipt date	April 15, 1983
Review by the National Heart, Lung, and Blood Advisory Council	September 22-24, 1983
Notification of applicants	September 28, 1983
Anticipated award date	September 30, 1983

E. Inquiries

Inquiries regarding this announcement may be directed to the program administrator:

Dr. Constance Weinstein
National Institute of Health
Federal Building - Room: 3C-06
Bethesda, Maryland 20205

Telephone: (301) 496-1081

ANNOUNCEMENT

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

RFA-NIH-NHLBI-DLD-83G-B

DEFENSE FUNCTIONS IN THE DEVELOPING RESPIRATORY SYSTEM

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Application Receipt Date: April 15,1983

I. BACKGROUND

The goal of this special grant program is to improve our understanding of the functional development of defense functions such as mucociliary clearance, phagocytosis, and local immune responses relative to host defense, in the tracheobronchial tree and at the alveolar level during fetal and postnatal life.

Studies on host-defense mechanisms in the respiratory system that are needed to maintain the lung in an aseptic state have been given considerable attention in adults in recent years. In the immature and developing respiratory system, however, our knowledge of such mechanisms is rather limited and incomplete.

The immature and developing lung is particularly vulnerable to microorganisms and other types of insults, and respiratory infections are among the most important contributors to morbidity of respiratory disorders in the first years of life. Current estimates indicate that the rate of bronchiolitis attacks may exceed 16 per year per hundred infants less than six months of age, and that the risk of hospitalization for these infants is in the order of 10 per 1,000 infants per year.

To further compound this problem it is now recognized that a significant number of very immature survivors of acute respiratory distress often have persistent complications such as secondary infections and recurrent bronchial obstruction. Although conclusive data are still lacking, it is suspected that respiratory illnesses in infancy and childhood may contribute to respiratory disorders and pulmonary function abnormalities later in life.

This program is described in the Catalog of Federal Domestic Assistance, No. 13.838, Lung Diseases. Awards will be made under the authority of the Public Health Service Act, Section 301 (42 USC 241) and administered under PHS grant policies and Federal regulations, most specifically 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

It is suspected that loss of ciliary movement and goblet cell function may occur as a result of repeated intubation and suctioning, and that such injuries may promote invasion of microorganisms that are difficult to eradicate. Furthermore, it has been noted that neonates who survice a long period of oxygen and ventilator dependency seem to be particularly at risk for acute pulmonary insufficiency, necessitating hospitalization, or for recurrent bronchiolitis during the first 2-3 years of life. Fundamental knowledge on the status of respiratory defense functions such as mucociliary clearance, alveolar macrophage phagocytosis and local immune responses as they apply to host defense, is currently lacking for the developing respiratory system.

Specifically, the degree of maturation of such defense functions at birth and during development, their responsiveness to challanges, and their vulnerability to insult are in need of investigation. Consequently, management and prevention of some of the most significant respiratory problems during development is mainly empirical. It is anticipated that a systematic approach to elucidating the functional development of such mechanisms may provide a scientific rationale for improved therapy and prevention.

II. OBJECTIVES AND SCOPE

The specific objective of this program is to encourage research on functional development of mucociliary clearance, phagocytosis, and local immune responses relative to host defense against infectious agents, in the tracheobronchial tree and at the alveolar level in fetal and postnatal life. For the purpose of this announcement, fetal life denotes a time not earlier than the third trimester. Investigations may be carried out in vivo or in vitro, on intact lungs, organ cultures or isolated cells, but must be designed so that meaningful extrapolations to the functional development of human lung defense are possible. Although defense functions during normal lung development should be a major theme of the applications, they may also include studies aimed towards understanding alterations in defense functions in response to insults or stimuli that are comparable to those likely to occur particularly in human infants and children receiving respiratory care.

Structural studies are encouraged if aimed towards elucidating structure-function relationships. Studies on the mature respiratory system may be included if the intent is to make relevant comparisons with the developing respiratory system, but major emphasis must be on the latter.

Research topics presented below are intended to provide a perspective of the scope of research that would meet the goals of this program. It is not required that all of these examples be included. Investigators are encouraged to consider other relevant approaches designed to expand our understanding of functional development of defense functions in the lung in fetal and postnatal life.

1) Alveolar macrophages and local immune responses.

Although alveolar macrophages constitute the major phagocytic defense of the lung, and although considerable research has been directed in the past to studies of the morphology, metabolism, and function of these mononuclear cells, little is known about their functional maturation during fetal and neonatal development including their capacity at different stages during development for phagocytosis and transportation of particles, and the influence of the environment (e.g., 0_2 concentration) on their function. It has been reported that the alveolar macrophages in the newborn are unable to respond to bacterial and viral challenges and lungs of infants have been reported to have lower phagocytic activity than those of adults. The reasons for this, however, remain unclear and studies are needed to elucidate ultrastructural and biochemical parameters related to the maturational development of alveolar macrophages and their phagocytic and microbicidal activities.

Development of local immune responses and the extent to which they may influence or modify the response of the immature lung to challenges from infectious agents are not well understood. Thus, although T and B cells are present as early as the first trimester, their appearance in the alveoli and their interaction with alveolar macrophages in relation to immunologic suppressor or stimulator reactions need investigation.

2) Mucociliary transport

The extent to which immaturity or impaired responses of mucociliary transport in the respiratory system contribute to the high rate of virulent respiratory infections in the premature and young infants and render them susceptible to other insults from the environment is poorly understood. Ciliated cells, ciliary motion and submucosal glands are present in utero well before the age of viability, but the effectiveness of the mucociliary transport mechanism in the immature respiratory system and its possible reaction to mechanical stimuli such as endotracheal intubation during lung development need elucidation. In addition, the possible relationship between the presence or absence of surfactant and alveolar-bronchiolar transport during lung development is unclear. It is known that factors from the environment may contribute to the depressed airway defense in adults. Irritants, for example, interacting with an altered airway epithelium may stimulate exposed sensory receptors resulting in increased vagal tone and chronic stimulation of submucosal glands. Altered mucus composition and secretion may compromise the function of the mucociliary transport system and increase the risk of intercurrent respiratory infection. Whether such processes occur during lung maturation and compromise defense functions in neonates and predispose to attacks of bronchiolitis is poorly understood.

III. EXCLUSIONS

Epidemiological studies and clinical trials will not be supported under this announcement; neither will studies on development of systemic or extrapulmonary immune defense functions, or studies on mechanism of pathogenicity of infectious agents.

IV. MECHANISM OF SUPPORT

The support mechanism for this program will be the traditional, individual research grant. Although approximately $500,000 for this program is included in the financial plans for fiscal year 1983, award of grants pursuant to this RFA is contingent upon receipt of funds for this purpose. It is anticipated that four to six grants will be awarded under this program. The specific amount to be funded will, however, depend on the merit and scope of the applications received and the availability of funds. Since a variety of approaches would represent valid responses to this announcement, it is anticipated that there will be a range of costs among individual grants awarded.

Upon initiation of the program, the Division of Lung Diseases (DLD) will sponsor periodic meetings to encourage exchange of information among investigators who participate in this program. In the preparation of the budget for the grant application, applicants should request travel funds for a one-day meeting each year, most likely to be held in Bethesda, Maryland. Applicants should also include a statement in their applications indicating their willingness to participate.

Applicants (who will plan and executive their own research programs) are requested to furnish their own estimates of the time required to achieve the objectives of the proposed research project; however, the award period for this activity should not exceed three years. At the end of the initial award period, renewal applications may be submitted for further competitive review through the regular grant program of the NIH. It is anticipated that support will begin on September 30, 1983.

The current policies and requirements that govern the research grant programs of the National Institutes of Health (NIH) will prevail, including the requirement for cost sharing.

V. REVIEW PROCEDURES AND CRITERIA

A. Review Method

All applications submitted in response to this RFA will be reviewed for scientific and technical merit by an initial review group, which will be convened by the Division of Extramural Affairs (DEA), National Heart, Lung, and Blood Institute (NHLBI), solely to review these applications. Upon receipt, applications will be reviewed for their responsiveness to the objectives of this RFA. If an application is judged unresponsive, the applicant will be contacted and given an opportunity to withdraw the application or to have it considered for the regular grant program of the NIH.

If a proposal submitted in response to this RFA is identical to a research grant application already submitted to the NIH for review, the applicant will be asked to withdraw the pending application before the new one is accepted. Simultaneous submission of identical applications will not be allowed.

B. Review Criteria

The factors to be considered in the evaluation of scientific merit of each applicant will be similar to those used in the review of traditional research project grant applications including the novelty, originality, and feasibility of the approach; the training, experience, and research competence of the investigator(s); the adequacy of the experimental design; the suitability of the facilities; and the appropriateness of the requested budget to the work proposed.

VI. METHOD OF APPLYING

A. Letter of Intent

Prospective applicants are encouraged to submit a one-page letter of intent that includes a brief synopsis of the proposed research and identification of any other participating institutions. Such letters are requested for the purpose of obtaining an indication of the number and scope of applications to be received. A letter of intent is not binding, and it will not enter into the review of any application subsequently submitted, nor is it a necessary requirement for application. This letter should be received no later than February 15, 1983, and sent to:

Charles L. Turbyfill, Ph.D.
National Heart, Lung, and Blood Institute
Westwood Building - Room 553
Bethesda, Maryland 20205

B. Format for Applications

Submit applications on form PHS 398, the application form for the traditional research project grant. This form is available in an applicant institution's office of sponsored research or from the Division of Research Grants (DRG). Use the conventional format for research project grant applications and ensure that the points identified in the section on "Review Procedures and Criteria" are fulfilled. To identify the application as a response to this RFA, check "yes" on item 2 of page 1 of the application and enter the title "DEFENSE FUNCTIONS IN THE DEVELOPING RESPIRATORY SYSTEM" and the RFA number NIH-NHLBI-DLD-83G-B.

C. Application Procedure

Send or deliver the completed application and six (6) signed, complete photocopies of it to:

Division of Research Grants
National Institutes of Health
Westwood Building - Room 5A15
Bethesda, Maryland 20205

Applications must be received by April 15, 1983. An application not received by this date will be considered ineligible.

D. Timetable

Letter of intent	February 15, 1983
Application receipt date	April 15, 1983
Review by National Advisory Council	September 1983
Anticipated award date	September 30, 1983

E. Inquiries

Inquiries regarding this announcement may be directed to the program administrator:

Bitten Stripp, Ph.D.
Chief, Structure and Function Branch
Division of Lung Diseases
National Heart, Lung, and Blood Institute
National Institutes of Health
Westwood Building - Room 6A03
Bethesda, Maryland 20205

Telephone: (301) 496-7171

ANNOUNCEMENT

REQUEST FOR RESEARCH GRANT APPLICATION: RFA

RFA-NIH-NHLBI-DHVD-83G-C

BIOBEHAVIORAL FACTORS AFFECTING HYPERTENSION IN BLACKS

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Application Receipt Date: April 15, 1983

I. PURPOSE

The Division of Heart and Vascular Diseases (DHVD), National Heart, Lung, and Blood Institute (NHLBI),invites grant applications for a single competition for support of research on the interaction of physiological and behavioral factors related to blood pressure variations and hypertension among Black populations. The major purpose of this special grant program is to gain basic information on blood pressure and other physiological response differences among population subgroups in the presence of controlled psychological stressors.

II. DISCIPLINES AND EXPERTISE

The interdisciplinary nature of this research makes appropriate combined expertise from biobehavioral research disciplines (psychophysiology, psychobiology, experimental psychology) in cooperation with biomedical disciplines (physiology, cardiology, neurobiology, genetics, and nutrition).

III. BACKGROUND

A. Administrative Background

As a component of the Clinical Applications and Prevention Program of the DHVD, the Behavioral Medicine Branch (DMB) encourages and administers programs of biobehavioral research related to cardiovascular health and disease issues. The program fosters maximum collaboration between the biomedical and behavioral science communmities on research problems of mutual concern including the use of behavioral techniques to elucidate basic mechanisms of cardiovascular control and identification of biobehavioral correlates of hypertension. Within that program objective, this solicitation is responsive to recommendations of the National Black Health Providers Task

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This program is identified in the Catalog of Federal Domestic Assistance No. 13.837, Heart and Vascular Diseases. Awards will be made under the authority of the Public Health Service Act, Section 301 (42 USC 241) and administered under PHS grant policies and Federal regulations, most specifically 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

Force on High Blood Pressure Education and Control (convened by NHLBI, October 1980) for research on the role of psychological and social stressors in the Black community.

Investigator-initiated research presently supported through the Behavioral Medicine Branch includes several projects investigating cardiovascular reactivity to controlled stressors in the laboratory, monitoring of blood pressure variations in response to identifiable stressful events in everyday life, and cardiovascular and neural differences in subgroups of subjects under behavioral challenges. A recent (1982) special announcement solicited proposals for biobehavioral research in animals on genetic and developmental factors in the etiology of hypertension. Encouragement of research addressing different subgroup responses relevant to hypertension in biobehavioral studies with human subjects is appropriate and within the scope of program emphasis.

B. Scientific Background

Hypertension prevalence rates differ among population subgroups with a significantly higher prevalence of the disorder reported among Blacks as compared to Whites in this country. Although the etiology of hypertension is not clearly understood, a broad spectrum of potential physiological, psychological and environmental contributors to the development of hypertension has been identified through scientific investigtions. Research evidence suggests physiological and behavioral/environmental factors interact to affect differences in disease prevalence among subgroups and that multifactorial studies of differences among subgroups such as Black and White populations have potential for elucidating the etiology of hypertension and its observed higher prevalance among Blacks.

Epidemiological studies have identified psychosocial and environmental stress factors as relevant and, in some case, primary variables in the development of hypertension. Dietary factors, particularly sodium intake in combination with a constitutional predisposition to salt sensitivity, have been investigated as contributing to increased blood pressure levels. Recent research explores the potential role of other nutrients (including potassium, calcium, magnesium) to elevated blood pressure and hypertension. Biobehavioral research on cardiovascular reactivity to laboratory psychological stressors reveals that behavioral and physiological interactions may be significant for explaining blood pressure variations. However, descriptive studies of environmental stressors in the development of hypertension rarely address interactions of psychological and physiological factors and few laboratory studies have conducted research on the effects of controlled stressors on specific population subgroups including Blacks.

Physiological studies suggest subgroup differences, such as increased sympathetic tone indicated by plasma renin or dopamine beta-hydroxylase levels, are linked to blood pressure variations. Sodium excretion and sodium/potassium ratio differences between Black and White populations have been reported. Recent work on "mild" hypertensives suggests that different mechanisms are significant for development of hypertension among subgroups characterized by differing physiological indicators. These scientific findings, however, do not explain blood pressure variations or hypertension prevalence differences. Evidence suggests a complex etiology for hypertension through which psychological and environmental factors interact with physiological variables resulting in different prevalence rates for subgroups including Black and White populations.

IV. OBJECTIVES

This special grant program is for the support of research on the interrelatedness of physiological mechanisms which in combination with behavioral factors could clarify the conditions for development of hypertension in groups with significant differences in prevalence of hypertension. Investigations directed toward differing responses of Black and White popultions or variables significant for Black populations are required by this special program.

V. SCOPE

The proposed research should be dedicated to augmenting existing knowledge of physiological responses of Blacks and Whites relevant to the development of hypertension and to gain basic information of subgroup responses to specific stressors relevant to blood pressure variations. Proposals involving interdisciplinry approaches in the development of interactive models of selected behavioral and physiological factors are encouraged. Models of the interaction of such factors should use defined variables, justify subject selection, and make use of appropriate biomedical and behavioral measurement techniques. While studies are expected to use controlled stressors within experimental designs, proposed research should indicate relevance to situations of naturally occurring stress.

Physiological factors applicable for proposed studies are those significant in the etiology of hypertension, including but not restricted to studies of nervous system activity and catecholamines; the renopressor or renin-angiotension system; the excretary function of the kidney; other hormonal and fluid balance controlling factors; and measures of cardiovascular reactivity. Dietary factors including sodium, sodium sensitivity, potassium and other nutrients are appropriate, as are other indicators used to differentiate among subgroups of hypertensives. Behavioral variables in proposed research designs may include laboratory challenges, controlled stressors or other emotional stimuli. Research supported under this program should include subjects and/or variables which will expand scientific knowledge of blood pressure variations among Black populations as a subgroup of interest.

Examples of appropriate research include, but are not limited to, the following: investigations of individual differences in behaviorally-induced cardiovascular reactivity among Black and White borderline hypertensives differing in autonomic functioning, studies of individuals differing in physiological indicators such as skin pigmentation, salt excretion, other nutrient levels or dietary intake patterns monitored for their responsiveness to laoratory psychological stimuli (including, but not limited to the cold pressor test, competitive stress, mental arithmetic, or task performance under laboratory-administered stressors); similar subgroups observed for physiological and psychological responses to salt loading; individual blood pressure variations and related physiological responses to stressor situations involving differences in coping strategies.

VI. EXCLUSIONS

Clinical trials or population survey research would not be supported through this solicitation. Educational approaches or comparison of treatments will be excluded from support. Proposals must be directed toward differentiating among factors significant to subgroups including Black populations to be considered appropriate. Although the research topic is interdisciplinary, it is not the intent of this request to solicit proposals for large studies encompassing a variety of essentially independent research projects (program projects).

VII. MECHANISM OF SUPPORT

The support mechanism for this program will be the traditional, individual, research-project grant. Although this program is included in the financial plan for fiscal year 1984, award of grants pursuant to this RFA is contingent upon receipt of funds for this purpose. It is anticipated that three to four grants will be awarded under this program. The specific amount to be funded will, however, depend on the merit and scope of the applications received and availability of funds. Since a variety of approaches would represent valid responses to this announcement, it is anticipated that there will be a range of costs among individual grants awarded.

Upon initiation of the program, the DHVD will sponsor periodic meetings to encourage exchange of information among investigators who participate in this program. In the preparation of the budget for the grant application, applicants should request travel funds for a two-day meeting each year, most likely to be held in Bethesda, Maryland. Applicants should also include a statement in their applications indicating their willingness to participate in such meetings and share information on their research methodology and progress.

Applicants, who will plan and execute their own research programs, are requested to furnish their own estimates of the time required to achieve the objectives of the proposed research project; however, the award period for this activity must not exceed three years. At the end of the initial award period, renewal applications may be submitted for further competitive review through the regular grant program of the National Institutes of Health (NIH). It is anticipated that support will begin on December 1, 1983. Should funding become available, awards may be authorized to begin at an earlier (September 30, 1983) date.

The current policies and requirements that govern the research grant programs of the NIH will prevail.

VIII. REVIEW PROCEDURES AND CRITERIA

A. Review Method

All applications responding to this RFA will be reviewed for scientific and technical merit by one initial review group, which will be convened by the Division of Extramural Affairs (DEA), NHLBI, solely to review these applications. Upon receipt, applications will be reviewed for their responsiveness to the objectives of this RFA. If an application is judged unresponsive, the applicant will be contacted and given an opportunity to withdraw the applicant or to have it considered in the regular research grant program of the NIH.

If a proposal submitted in response to this RFA is identical to a research grant application already submitted to the NIH for review, the applicant will be asked to withdraw the pending application before the new one is accepted. Simultaneous submnission of identical applications will not be allowed.

B. Review Criteria

The factors to be considered in the evaluation of scientific merit of each application will be similar to those used in the review of traditional research-project grant applications, including the novelty, originality, and feasibility of the approach; the training, experience, and research competence of the investigator(s); the adequacy of the experimental design; the suitability of the facilities; and the appropriateness of the requested budget to the work proposed. An assessment of the importance of the proposed research to the objectives of this RFA and relevance to its goals will be important review considerations.

IX. METHOD OF APPLYING

A. Letter of Intent

Prospective applicants are encouraged to submit to the Review Branch of the Institute a one-page letter of intent that includes a brief synopsis of the proposed research and identification of any other participating institutions. The Institute requests such letters for the purpose of providing an indication of the number and scope of applications to be expected. A letter of intent is not binding, and it will not enter into the review of any application subsequently submitted, nor is it a necessary requirement of application. This letter should be received no later than February 15, 1983. Letters of intent should be sent to:

Dr. Charles L. Turbyfill
National Heart, Lung, and Blood Institute
Westwood Building - Room 553
Bethesda, Maryland 20205

B. Format for Applications

Submit applications on form PHS 398, the application form for the traditional research-project grant. This form is available in an applicant institution's office of sponsored research or business office or from the Division of Research Grants (DRG). Use the conventional format for research-project grant applications and ensure that the points identified in the Section on "Review Procedures and Criteria" are fulfilled.

To identify the application as a response to this RFA, check "yes" on Item 2 of page 1 of the application and enter the title "BIOBEHAVIORAL FACTORS AFFECTING HYPERTENSION IN BLACKS" and the RFA number NIH-NHLBI-DHVD-83G-C.

C. Application Procedure

Send or deliver the completed application and six (6) signed, exact photocopies of it it:

Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
Bethesda, Maryland 20205

Send an additional twenty (20) copies of the application to:

Review Branch, DEA
National Heart, Lung, and Blood Institute
National Institutes of Health
Westwood Building - Room 5A15
Bethesda, Maryland 20205

Applications must be received by April 15, 1983. An application not received by this date will be considered ineligible for this program, but after discussion with the applicant, it may be considered as a regular research-project grant application.

Timetable:

Letter of intent	February 15, 1983
Application receipt date	April 15, 1983
Review by the National Heart, Lung, and Blood Advisory Council	September 22-24, 1983
Notification of applicants	September 28, 1983
Anticipated award date	December 1, 1983

D. Inquiries

Inquiries regarding this announcement may be directed to the program administrator:

Dr. Katrina W. Johnson
National Institutes of Health
Federal Building - Room 604
Bethesda, Maryland 20205

Telephone: (301) 496-9380

ANNOUNCEMENT

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

RFA-NIH-NHLBI-DHVD-83G-D

CARDIAC HYPERTROPHY AND FAILURE IN CHRONIC HYPERTENSION

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Application Receipt Date: April 15, 1983

I. PURPOSE

The Division of Heart an Vascular Diseases (DHVD), National Heart, Lung, and Blood Institute (NHLBI), invites grant applications for support of research on cardiac hypertrophy in chronic hypertension. The purpose of this special grant program is to expand the study of the transition from normal cardiac structure and function to cardiac hypertrophy and cardiac failure in chronic systemic hypertension, with special emphasis on the mechanisms responsible for these changes. Applications received in response to this request will participate in a single competition.

II. DISCIPLINES AND EXPERTISE

Among the disciplines and expertise that may be appropriate for this research program are molecular biology, physiology, protein and collagen chemistry, pathology, ultrastructure, and clinical cardiology.

III. BACKGROUND

The Hypertension and Kidney Diseases Branch, of the DHVD, designs and administers programs of research and development seeking to understand the etiology of essential hypertension and the impact of hypertension on organ systems. The program fosters the development of new knowledge and the translation of results into methods for clinical application.

The Hypertension and Kidney Diseases Branch currently support research linking cardiac structure and function to hypertension, but the amount of research dealing with the effects of long-term, chronic hypertension is limited.

This program is identified in the Catalog of Federal Domestic Assistance No. 13.837, Heart and Vascular Diseases. Awards will be made under the authority of the Public Health Service Act, Section 301 (42 USC 241) and administered under PHS grant policies and Federal regulations, most specifically 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

Two recently held NHLBI-sponsored workshops assessed the status of research relating to cardiac hypertrophy and cardiac failure, the Workshop on Advanced Heart Failure in Spring 1981, and the Workshop on Ventricular Hypertrophy in Hypertension in Fall 1981. This RFA is based upon recommendations arising from these workshops. It was identified as a high priority project by the Arteriosclerosis, Hypertension, and Lipid Metabolism Advisory Committee at its May 1982 meeting.

IV. OBJECTIVES AND SCOPE

The objective of this special grant program is to stimulate the development of research to characterize the transition from normal cardiac structure and function to cardiac hypertrophy and cardiac failure in chronic hypertension. There is special interest in clarifying the mechanisms by which these effects are produced, and in identifying stages in the process where changes are "reversible" and where they are "irreversible." A broad range of research interest areas will be responsive to this initiative, including hemodynamic, morphological, physiological, and biochemical changes affecting stromal, muscular and vascular components of the heart.

This special research program will involve predominantly animal models of chronic systemic hypertension. Scientific advances, such as in cardiac physiology, in the biochemistry of connective tissue synthesis, in the ability to assess ventricular function, and in understanding of drugs which improve cardiac contraction, are available to be applied to these models. Experimental models other than those of chronic hypertension will be acceptable only if their relevance to hypertensive-induced cardiac hypertrophy can be shown. Because this initiative seeks to clarify basic mechanisms, it is anticipated that proposals will be based principally on animal experimentation. However, the Branch does not wish to rule out the possibility that a proposal based on human subjects could be responsive to this announcement.

Applications are sought from individuals and from groups of investigators. Interdisciplinary proposals are encouraged, but such proposals must be carefully focused. If collaborative arrangements through subcontracts with other institutions are planned, NHLBI staff should be consulted regarding the appropriate procedures.

V. EXAMPLES OF RESEARCH TOPICS

The following lines of research are presented as examples only, and do not exhaust the many opportunities for productive research. They are not listed in order of importance:

- The fibrous skeleton of the heart and its influence on the systolic and diastolic functions of the heart require further characterization. This field is of particular importance because the complex network of collagen bundles in the heart that interconnects the myocytes and capillaries and orders the myocytes into groups, is altered in disease states. There is as yet no organized body of information to relate abnormalities of collagen synthesis to altered ventricular function in cardiac hypertrophy. Closely linked to the study of the connective tissue is the evaluation of the "non-muscle space" in the heart, particularly as regards the organization of the microvascular bed, the lymphatics, and connective tissue matrix.

- The study of myocardial metabolism has been undertaken mostly in non-hypertensive conditions. It is important to ascertain whether substrates and types of proteins (both contractile and noncontractile) are different between genetic and non-genetic forms of hypertension. Evidence has been developed that protease activity is greatly increased in the myocardium during the development of hypertensive hypertrophy. The systems responsible for this increased activity and their involvement in controlling the rate of proteolysis need to be further defined since an imbalance in them can account for changes in cardiac muscle size and protein composition, as well as result in changes in contractile activity and metabolic function.
- Analysis of catecholamine turnover in the myocardium is important. A highly suggestive body of evidence has been developed recently, to the effect that adrenergic influences play a role in modulating structural responses of the heart and of resistance vessels to hypertension.
- There is interest both in the transition to hypertrophy and in the reverse process. Through timed interventions at various stages of the transition and by correlation of the morphological, histological, biochemical, and physiological changes that occur, it may be possible to gain new insights into the fundamental properties of the myocardium in heart failure, and to identify the points of irreversibility in the pathophysiological process.

  The presently used animal models of long-term, chronic hypertension are limited and new models would be welcome. How long a given animal must remain hypertensive before initiation of anatomical and biochemical changes is not established. Thus, the early stages of the project could be concerned with long-term model development and characterization.

VI. EXCLUSIONS

No support will be provided for research in cardiac hypertrophy or failure resulting from known initiating factors other than systemic hypertension, unless the relevance to systemic hypertension-induced conditions can be shown. It is not the intent of this request to solicit proposals resembling program projects. However, in some instances the need for several skills will be recognized. Such collaborative research should be justified in the proposal accordingly.

VII. MECHANISM OF SUPPORT

The support mechanism for this program will be the traditional, individual, research project grant. Although this solicitation is included in the plans for Fiscal Year 1984, support of grants pursuant to this request for applications is contingent upon ultimate receipt of appropriate funds for this purpose. It is anticipated that up to six grants will be awarded, however, the specific number will be influenced by the amount of funds available to the Division, by the overall merit of proposals, and by their critical relevance to the program objectives. A variety of approaches will be responsive to this announcement; accordingly, it is anticipated that there will be a range of costs among individual grants awarded.

Upon initiation of the program, the DHVD will sponsor periodic meetings to encourage exchange of informtion among participating investigators. In the preparation of the budget for the grant application, applicants should request travel funds for a two-day meeting each year, most likely to be held in Bethesda, Maryland. Applicants should also include a statement in their applications indicating their willingness to participate in such meetings.

Applicants, who will plan and execute their own research programs, are requested to furnish their own estimates of the time required to achieve the objectives of the proposed research project; however, the award period for this activity will not exceed five years. At the end of the initial award period, renewal applications may be submitted for further competitive review through the regular grant program of the NIH. It is anticipated that support will begin on December 1, 1983. However, if funds are available an earlier start date could be authorized.

The current policies and requirements that govern the research grant programs of the NIH will prevail.

VIII. REVIEW PROCEDURES AND CRITERIA

A. Review Method

All applications responding to this RFA will be reviewed for scientific and technical merit by one initial review group, which will be convened by the Division of Extramural Affairs (DEA), NHLBI, solely to review these applications. Upon receipt, applications will be reviewed for their responsiveness to the objectives of this RFA. If an application is judged unresponsive, the applicant will be contacted and given an opportunity to withdraw the application or to have it considered for the regular research grant program of the NIH. If a proposal submitted in response to this RFA is identical to a research grant application already submitted to the NIH for review, the applicant will be asked to withdraw the pending application before the new one is accepted. Simultaneous submission of identical applications will not be allowed.

B. Review Criteria

The factor to be considered in the evaluation of scientific merit of each application will be similar to those used in the review of traditional research-project grant applications; the novelty, originality, and feasibility of the approach; the training, experience, and research competence of the investigator(s); the adequacy of the experimental design; the suitability of the facilities; and the appropriateness of the requested budget to the work proposed. An additional criterion will be the importance of the proposed work to the objectives of this RFA.

IX. METHOD APPLYING

A. Letter of Intent

Prospective applicants are encouraged to submit to the Review Branch of the Institute a one-page letter of intent that includes a brief synopsis of the proposed research and identification of any other participating institutions. The Institute requests such letters for the purpose of providing an indication of the number and scope of applications to be received. A letter of intent is not binding, and it will not enter into the review of any application subsequently submitted, nor is it a necessary requirement for application. This letter should be received no later than February 15, 1983, and sent to:

Dr. Charles L. Turbyfill
National Heart, Lung, and Blood Institute
Westwood Building - Room 553
Bethesda, Maryland 20205

B. Format for Applications

Submit applications on form PHS 398, the application form for the traditional research-project grant. This form is available in an applicant institution's office of sponsored research or business office or from the Division of Research Grants (DRG). Use the conventional format for research-project grant applications and ensure that the points identified in the Section on "Review Procedures and Criteria" are fulfilled.

To identify the application as a response to this RFA, check "yes" on Item 2 of page 1 of the application and enter the title "CARDIAC HYPERTROPHY AND FAILURE IN CHRONIC HYPERTENSION" and the RFA number NIH-NHLBI-DHVD-83G-D.

C. Application Procedure

Send or deliver the completed application and six (6) signed, exact photocopies of it to:

Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
Bethesda, Maryland 20205

Send an additional twenty (20) copies of the application to:

Review Branch, DEA
National Heart, Lung, and Blood Institute
National Institutes of Health
Westwood Building - Room 5A15A
Bethesda, Maryland 20205

Applications must be received by April 15, 1983. An application not received by this date will be considered ineligible, but after discussion with the applicant, it may be considered as a regular research-project grant application.

D. Timetable

Letter of intent	February 15, 1983
Application receipt date	April 15, 1983
Review by the National Heart, Lung, and Blood Advisory Council	September 22-24, 1983
Notification of applicants	September 28, 1983
Anticipated award date	December 1, 1983

E. Inquiries

Inquiries regarding this announcement may be directed to the program administrator:

Dr. John B. Dunbar
National Institutes of Health
Federal Building - Room 4C08
Bethesda, Maryland 20205

Telephone: (301) 496-1857

ANNOUNCEMENT

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

RFA-NIH-NHLBI-DHVD-83G-E

DYSRHTHMIAS IN THE DEVELOPING AND IMMATURE HEART

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Application Receipt Date: April 15, 1983

I. PURPOSE

The Division of Heart and Vascular Diseases (DHVD), National Heart, Lung, and Blood Institute (NHLBI), invites grant applications for support of research in developmental electrophysiology and control of dysrhythmias in the young. Knowledge gained by studies on the immature and developing conduction system approached from basic cellular and from clinical perspectives should lead to more appropriate care of the pediatric cardiovascular patient. Applications received in response to this request will participate in a single competition.

II. DISCIPLINES AND EXPERTISE

Disciplines and expertise appropriate for this research program include embryology, pharmacology, electrophysiology, pediatric cardiology, biochemistry, physiology, pathology and biophysics.

III. BACKGROUND

There is incomplete knowledge of the etiology, pathophysiology, and rational therapeutic approach to cardiac dysrhythmias in children.

The prevalence and incidence of dysrhythmia and conduction defects in children are not known but one large study found 2 per cent of randomly selected children had some form of dysrhythmia. Ambulatory monitoring has revealed conduction abnormalities and dysrhythmias to be more prevalent than was previously thought. Whereas some pediatric dysrhythmias are benign and transient, others may be serious or even fatal. Although effort has been expended to define normal electrophysiologic parameters for infants and children, pediatric dysrhythmias and conduction disturbances have not been studied systematically. Some forms of congenital or acquired heart disease are especially susceptible to early or late postoperative dysrhythmias. The number of children with congenital heart disease

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This program is described in the Catalog of Federal Domestic Assistance No. 13.837, Heart and Vascular Diseases. Awards will be made under the authority of the Public Health Service Act, Section 301 (42 USC 241) and administered under PHS grant policies and Federal regulations, most specifically 42 CFR Part 52 and 45 CRF Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

who survive surgery is increasing, and with their longer survival, an increasing incidence of dysrhythmia is seen. More is known about serious conduction abnormalities and dysrhythmia following surgery for d-transposition of the great vessels (d-TGA) and tetralogy of Fallot (TOF) than any other congenital lesions, yet only basic descriptive and natural history questions have been examined. Each year, 1000 children with d-TGA and 5000 with TOF successfully undergo surgical correction. Follow up studies reveal that most of these patients subsequently develop conduction disturbances. The significance of these different disturbances and their relationship to sudden death is not clear. These children are now surviving into adulthood; the incidence and significance of rhythm disturbances in adult survivors of surgical correction of congenital heart disease is unknown. Virtually nothing is known about dysrhythmias in other congenital lesions.

The etiology and mechanisms of acquired or naturally occurring arrhythmias in the developing and maturing heart are unknown. Additionally there is a paucity of information regarding the pharmacokinetics and pharmacodynamics of conventional and investigational antiarrhythmic agents in neonates and children. This information is needed for safe, effective therapy. No prior organized program of research in the area of dysrhythmia in the young has been undertaken.

IV. OBJECTIVES

The objectives of this solicitation are to stimulate research into the etiology, pathophysiology and treatment of rhythm disturbances in the developing and young heart. The topic requires a multifaceted approach encompassing biochemistry, biophysics, physiology and pharmacology to evaluate abnormalities of impulse generation and conduction in basic cellular systems as well as intact animal and clinical studies.

V. SCOPE

Fundamental electrophysiologic studies in adults are well established, but little is known about how development influences impulse generation, conduction or mechanisms of re-entry. There is great need for further information on these issues.

Experiments at the cellular level have demonstrated differences in the action potential configuration in the fetal, neonatal and adult heart. The neonatal cardiac cell appears to be less sensitive to pharmacologic intervention than the mature cell; whether this is due to differences in cellular drug metabolism and distribution, immaturity of receptors, transmembrane permeability or other factors is not known. Greater understanding of the cellular events in the developing cardiac cell, and their differences from those of the mature cell are needed.

The neonatal myocardium differs structurally and biochemically from the adult myocardium; the neonate has a different capacity for conjugating, detoxifying and excreting drugs, and extracellular fluid volume in neonates is proportionately greater than in adults. There appear to be differences between children and adults in the distribution, bioological half life, plasma half life and even the metabolites for some of the major anti-arrhythmic agents. There is almost no information about these differences with the newer agents. Therefore studies of these and other variables (such as effects on cardiovascular function and electrophysiologic variables) at different stages of development from the fetus to the adult are needed. These studies can be done in great detail in experimental animals, and where appropriate, confirmed in patients of various ages. This would permit identification of approprite pharmacologic regimens for clinical treatment.

VI. EXCLUSION

Clinical trials or clinical drug validation studies would not be supported through this special solicitation. Studies of sudden infant death syndrome (SIDS) are also not appropriate for this solicitation. Although the research topic may be multidisciplinary, it is not the intent of this request to solicit proposals for large studies encompassing a variety of essentially independent research projects (program projects).

VII. MECHANISM OF SUPPORT

The support mechanism for this program will be the traditional, individual, research project grant. Although $600,000 in total costs for this program are included in the fiscal plans for fiscal year 1983, award of grants pursuant to this RFA is contingent upon receipt of funds for this purpose. Depending on the merit of the application, 5 or 6 applications for a three-year period will be funded. Upon initiation of the program, the Cardiac Diseases Branch (CDC), DHVD, will sponsor meeting to encourage exchange of information among investigators who participate in this program. In the preparation of the budget of the grant application, applicants should request travel funds for a two-day meeting on this topic each year, most likely to be held in Bethesda, Maryland. Applicants should also include a statement in their application indicating their willingness to participate in such meetings. At the end of the initial award period, renewal applications may be submitted for competitive renewal through the regular grant program of the NIH. Since a variety of approaches would represent valid responses to this announcement, it is anticipated that there will be a range of costs amongst the individual grants awarded.

All current policies and requirements that govern the research grant programs of the PHS will apply.

VIII. REVIEW PROCEDURES AND CRITERIA

A. Review Method

All applications responding to this RFA will be reviewed for scientific and technical merit by an initial review group, which will be convened by the Division of Extramural Affairs (DEA), NHLBI, solely to review these applications. Upon receipt, applications will be reviewed for their responsiveness to the objectives of this RFA. If an application is judged unresponsive, the applicant will be contacted and given an opportunity to withdraw the application or to have it considered for the regular research grant program of the NIH.

If a proposal submitted in response to this RFA is identical to a research grant application already submitted to the NIH for review, the applicant will be asked to withdraw the pending application before the new one is accepted. Simultaneous submission of identical applications will not be allowed.

B. Review Criteria

The factors to be considered in the evaluation of scientific merit of each application will be similar to those used in the review of traditional research-project grant applications; the novelty, originality, and feasibility of the approach; the training, experience, and research competence of the investigator(s); the adequacy of the experimental design; the suitability of the facilities; and the appropriateness of the requested budget to the work proposed. An additional criterion will be the importance of the proposed work to the objectives of this RFA.

IX. METHOD OF APPLYING

A. Letter of Intent

Prospective applicants are encouraged to submit to the Review Branch of the Institute a one-page letter of intent that includes a brief synopsis of the proposed research and identification of any other participating institutions. The Institute requests such letters for the purpose of providing an indication of the number and scope of applications to be received. A letter of intent is not binding, and it will not enter into the review of any application subsequently submitted, nor is it a necessary requirement for application. This letter should be received no later than February 15, 1983 and sent to:

Dr. Charles L. Turbyfill
National Heart, Lung, and Blood Institute
Westwood Building - Room 553
Bethesda, Maryland 20205

B. Format for Applications

Submit applications on form PHS 398, the application form for the traditional research-project grant. This form is available in an applicant institution's office of sponsored research or business office or from the Division of Research Grnts (DRG). Use the conventional format for research-project grant applications and ensure that the points identified in the Section on "Review Procedures and Criteria" are fulfilled.

To identify the application as a response to this RFA, check "yes" on Item 2 of page 1 of the application and enter the title "DYSRHTHMIAS IN THE DEVELOPING AND IMMATURE HEART" and the RFA number NIH-NHLBI-DHVD-83G-E.

C. Application Procedure

Send or deliver the completed application and six (6) signed, exact photocopies of it to:

Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
Bethesda, Maryland 20205

Send an additional twenty (20) copies of the application to:

Review Branch, DEA
National Heart, Lung, and Blood Institute
National Institutes of Health
Westwood Building - Room 5A15
Bethesda, Maryland 20205

Applications must be received by April 15, 1983. An application not received by this date will be considered ineligible, but after discussion with the applicant, it may be considered as a regular research-project grant application.

D. Timetable

Letter of intent	February 15, 1983
Application receipt date	April 15, 1983
Review by the National Heart, Lung, and Blood Advisory Council	September 22-24, 1983
Notification of applicants	September 28, 1983
Anticipated award date	September 30, 1983

E. Inquiries

Inquiries regarding this announcement may be directed to the program administrator:

Zena McCallum
National Institutes of Health
Federal Building - Room 3C06
Bethesda, Maryland 20205

Telephone: (301) 496-1081

ANNOUNCEMENT

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

RFA-NIH-NHLBI-DBDR-83G-F

RHEOLOGICAL STUDIES IN SICKLE CELL DISEASE

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Application Receipt Date: April 15, 1983

I. PURPOSE

The Division of Blood Diseases and Resources (DBDR), National Heart, Lung, and Blood Institute (NHLBI), invites grant applications for a single competition for support of research designed to clarify rheological aspects of sickle cell disease. The submission of applications with new, especially interdisciplinary approaches, by investigator who may not have previously worked in sickle cell disease is specifically encouraged. The section on Program Scope, based on the program objectives presented, is meant to suggest, rather than circumscribe, the range of approaches of interest for this RFA. No one laboratory is expected to cover the entire Program Scope. A variety of approaches could be considered as valid responses to this announcement.

II. DISCIPLINES AND EXPERTISE

Among the disciplines and expertise that may be appropriate for this research program are rheology, engineering, hemoglobin chemistry, molecular and cell biology, membrane biochemistry, and clinical expertise in hematology.

III. ADMINISTRATIVE BACKGROUND

The Sickle Cell Disease Branch of the Division of Blood Diseases and Resources, sponsors fundamental and clinical research grants and contracts related to the pathophysiology of clinical syndromes caused by sickle hemoglobin. In addition, studies are supported which utilize anatomical, biochemical, biophysical, physiological, and clinical approaches to increase our understanding of the nature, cause, diagnosis and treatment of sickle cell disease.

Several projects in this and related areas are supported by investigator-initiated grants. Research topics include nuclear magnetic resonance techniques for investigating the structure-function relationships in normal and sickle cell

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This program is described in the Catalog of Federal Domestic Assistance No. 13.839, Blood Diseases and Resources. Awards will be made under the Public Health Service Act, Section 301 (42 USC 241) and administered under PHS grant policies and Federal regulations, most specifically 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

hemoglobins; the use of crystallography and electron microscopy techniques in order to determine the molecular structure of sickle cell fibers; biophysical approaches to erythrocyte sickling; and erythrocyte-endothelial interactions in sickle cell disease. In addition, special initiatives sponsored by the Institute have led to the support of investigators attempting to develop an intravascular system for assaying characteristics of sickle erythrocytes in laboratory animal systems. For example, two grants were awarded in 1979 to (1) study ways of increasing our understanding of the pathophysiology of sickle cell anemia through a systematic *in vivo* study of the behavior of sickle erythrocytes; (2) employ the intravascular system for the evaluation of the *in vivo* effectiveness of various drugs known to inhibit sickling *in vitro*; and (3) correlate *in vitro* and *in vivo* rheological chanf the behavior of sickle erythrocytes; (2) employ the intravascular system for the evaluation of the *in vivo* effectiveness of various drugs known to inhibit sickling *in vitro*; and (3) correlate *in vitro* and *in vivo* rheological changes with manifestations of tissue damage as an explanation of the pathophysiology of sickle cell disease. In each of the two grants, emphasis was on the rheologic behavior of sickle erythrocytes.

IV. SCIENTIFIC BACKGROUND

Since the initial work of Ham and Castle in 1940, it has been evident that alterations of the biophysical properties of sickle erythrocytes affect their ability to flow in the microvasculature and are important elements in the pathogenesis of sickle cell disease and its complications. Numerous *in vitro* studies on blood from sickle cell patients have established that the deoxygenated sickle cell is 10 to 25 times more rigid than the normal hemoglobin AA cell. When measured in bulk-flow viscometric systems, blood from sickle cell disease patients has a higher than normal viscosity even when oxygenated. In Hgb SC, S + thal and SF double heterozygous states, viscosities are intermediate between those of SS and AA cells and correlate with the clinical severity of disease. In Hgb SC disease, the high hematocrit viscosity effect influences the propensity for vascular occlusions in the ocular fundus and aseptic necrosis of bone.

Techniques designed to measure red cell deformability (capacity of blood to traverse micropore filters) have demonstrated a marked decrease in the filterability of sickle cell blood under both ambient and deoxygenated conditions. The principal contributor in the oxygenated state appears to be the *irreversible sickled cell* (ISC), a membrane-damaged cell which retains its rigid sickle shape even under oxygenation. These irreversibly sickled cells, which number as many as 35 percent of the total erythrocytes of a patient with sickle cell disease, owe a part of their rigidity to the high corpuscular hemoglobin concentration.

Furthermore, the deformability and rheologic characteristics of sickle erythrocytes, both ISC and non-ISC, have been studied in a variety of systems including viscometric, cell filtration, and artificial blood flow devices. Such studies have shown that the critical oxygen tension for altering the rheologic properties of sickle cells occurs in the range of 60 to 80 mm Hg. This critical $p0_2$ range is substantially above that encountered at the venous end of the capillary bed (40 mm Hg to as low as 18 mm Hg in the coronary sinus). Observations in the capillary beds of experimental animal models and the "apparent" frequency of microvascular occlusion in patients would suggest that sickle cells generally escape entrapment within the microvasculature before a critical $p0_2$ is reached. Such considerations have led molecular biologists to propose the "kinetic hypothesis" for sickling vaso-occlusion. This hypothesis simply states that when capillary transit time is shorter than sickling time, vaso-occlusion does not occur. Conversely, when capillary transit time is delayed so that it exceeds sickling time, the cell will become rigid within the capillary and initiate vaso-occlusion. Conditions which can retard or impede the capillary transit time of individual SS erythrocytes are manifold. Blockage of the capillary microcirculation at bifurcation points by ISC's hinders the flow of non-ISC's across a given capillary bed causing them to undergo intravascular sickling. Capillary edema, inflammation, and the effect of vasoactive substances may influence the capillary flow rate and substrata in such a way as to prolong transit time. An alternative model, which stresses the equilibrium amounts of polymer at oxygen saturation values in the microcirculation, rather than the kinetics of sickling and possible obstruction to flow at the arteriolar side of the circulation, has also been proposed.

Several recent observations concerning the propensity of sickle cells to adhere to endothelial cells have raised the question of whether these adherent sickle cells, both ISC and non-ISC, can retard blood flow, initiating vaso-occlusion and inducing endothelial damage and microvascular pathology. Both physiologic and ultrastructural methods of assessment have shown that microvascular beds and their individual cell components are capable of active responses to both physiologic and pathologic stimuli. Constrictor substances, such as vasoactive amines, and proteins are capable of inducing dramatic alterations in the blood flow to a given capillary bed. The endothelial cell undergoes significant pathologic alteration in response to stimuli such as hypoxia. With both acute and sustained low oxygen tensions, endothelial cells develop vacuolization and a microvillous luminal surface capable of further impeding blood flow. Thus, since impedence of blood flow is the key rheologic determinant of sickle cell disease, and both in vitro and in vivo evidence points to a wide spectrum of abnormalities in the sickle cell, the capillary bed, and the endothelial cells, it would appear that new research initiatives to elucidate rheologic and microvascular mechanisms in sickle cell disease should be pursued.

Recent studies indicate a strong correlation between adhesion of sickle cells to the endothelium and the clinical severity of the disease. However, as yet no in vitro test has been successful in quantitating the physical properties of the adhesion.

V. OBJECTIVES

The fundamental pathophysiology of sickle cell disease involves a disturbance of microvascular flow. The intracellular gelation of sickle hemoglobin appears to be the critical factor in affecting flow through the microcirculation, although other processes may also contribute. Therefore, an important facet of future research in sickle cell disease is the study of the passage of sickle cells through different regions of the microcirculation under a variety of physiologically relevant conditions. The specific objectives of this solicitation are to:

- develop models to study normal and sickle erythrocyte deformability and flow;
- develop an understanding of the influence of the physical state of intracellular hemoglobin on the rheologic properties of sickle erythrocytes;

- increase knowledge of the structure and function of the erythrocyte membrane in relationship to its direct involvement in the rheologic pathology of sickle cell anemia;
- develop *in vitro* flow models, with complex geometry, that incorporate such features as branching, bending, bifurcation, and a length and diameter approximating those of the microcirculation;
- develop experimental systems using *ex vivo* or *in vivo* microcirculatory beds of varying order and geometry in which rheologic and physiologic variables such as pressure, flow, oxygen tension, and hematocrit can be controlled and measured;
- elucidate the mechanisms of control and anatomical sites of microvascular obstruction in sickle cell disease, including neural and hormonal control, and the function of plasma factor, leukocyte and platelets in microvascular occlusion; and
- develop techniques for studying the microvasculature in normal human subject and sickle cell patients in order to quantitate rheologic and physiologic variables.

VI. SCOPE

The central derangement in sickle cell disease appears to be an abnormality of microcirculatory flow caused by the sickled erythrocyte. To understand events that lead to the chronic anemia and interfere with tissue perfusion, better comprehension of red cell rheology and microcirculatory dynamics in sickle cell anemia is necessary.

The mechanism of intracellular polymerization of sickle hemoglobin and its effects on the properties of the erythrocyte are areas for further investigation. Studies of the internal viscosity of the erythrocyte, change in the structure and function of the erythrocyte membrane, and alterations in the deformability and flow properties of whole erythrocytes under various conditions of hematocrit, oxygen saturation (degree of hemoglobin ligation), temperature, intracellular pH, osmolarity and other relevant variables are necessary in sickle cell disease rheology. These studies should be done under experimental conditions that best simulate physiological conditions.

Information on irreversibly sickled cells and the interaction of sickle erythrocytes with numerous blood components as well as with other cells including leukocyte and platelets is lacking. The significance of cellular interactions with the endothelium and modulating factors of these interactions, as fibrinogen or bigronectin, are relevant subjects for study since there is evidence that adherence to endothelial cells correlates with clinical severity. Interaction of hemoglobin with the red cell membrane, the structure and function of membrane proteins and lipids, and physiological processes related to cellular dehydration and ion fluxes are also of potential relevance. Considerable importance is placed on the evaluation of the pathophysiological role in all such studies.

Recent work in circulatory physiology using noninvasive methods of measuring organ integrity and blood flow, such as NMR imaging, ultrasound and Doppler measurements, laser and photomicroscopy, and new method of measuring physiology of whole organs, (for example, position emission tomography), suggests new approaches to rheologic studies of experimental animals or, more important, to the evaluation of organ and tissue blood flow in normal individuals and sickle cell patients. It is expected that such methods will eventually provide objective means for evaluating the severity of sickle cell anemia, studying the clinical heterogeneity of the disease and evaluating potential therapeutic agents.

Interdisciplinary approaches are encouraged, but grant applications should be tightly focused. If collaborative arrangements through subcontracts with other institutions are planned, consult NHLBI staff regarding procedures.

VII. EXCLUSIONS

No support will be provided for major instrument research or development. Clinical trials or clinical validation of currently available instruments would not be suported through this special solicitation. Although the research topic may be multidisciplinary, it is not the intent of this request to solicit proposals for large studies encompassing a variety of essentially independent research projects (program projects).

VIII. MECHANISM OF SUPPORT

The support mechanism for this program will be the traditional, individual, research project grant. Although $500,000 for this program is included in the financial plans for fiscal year 1983, award of grants pursuant to this RFA is contingent upon receipt of funds for this purpose. It is anticipated that three to five grants will be awarded under this program. The specific amount to be funded will, however, depend on the merit and scope of the applications received and the availability of funds. Since a variety of approaches would represent valid responses to this announcement, it is anticipated that there will be a range of cost among individual grants awarded.

Upon initiation of the program, the DBDR will sponsor periodic meetings to encourage exchange of information among investigators who participate in this program. In the preparation of the budget for the grant application, applicants should request travel funds for a two-day meeting each year, most likely to be held in Bethesda, Maryland. Applicants should also include a statement in their applications indicating their willingness to participate in such meetings.

Applicants, who will plan and execute their own research programs, are requested to furnish their own estimates of the time required to achieve the objectives of the proposed research project; however, the award period for this activity must not exceed three years. At the end of the initial award period, renewal applications may be submitted for further competitive review through the regular grant program of the NIH. It is anticipated that support will begin on September 30, 1983.

The current policies and requirements that govern the research grant programs of the NIH will prevail.

IX. REVIEW PROCEDURES AND CRITERIA

A. Review Method

All applications responding to this RFA will be reviewed for scientific and technical merit by an initial review group, which will be convened by the Division of Extramural Affairs (DEA), NHLBI, solely to review these applications. Upon receipt, applications will be reviewed for their responsiveness to the objectives of this RFA. If an application is judged unresponsive, the applicant will be contacted and given opportunity to withdraw the application or to have it considered for the regular research grant program of the NIH.

If a proposal submitted in response to this RFA is identical to a research grant application already submitted to the NIH for review, the applicant will be asked to withdraw the pending application before the new one is accepted. Simultaneous submission of identical applications will not be allowed.

B. Review Criteria

The factors to be considered in the evaluation of scientific merit of each application will be similar to those used in the review of traditional research project grant applications. These include the novelty, originality and feasibility of the approach; the training, experience, and research competence of the investigator(s); the adequacy of the experimental design; the suitability of the facilities; and the appropriateness of the requested budget to the work proposed. An additional criterion will be the importance of the proposed research to the objectives of this RFA.

X. METHOD OF APPLYING

A. Letter of Intent

Prospective applicants are encouraged to submit to the Review Branch of the Institute a one-page letter of intent that includes a brief synopsis of the proposed research and identification of any other participating institutions.

The Institute requests such letters for the purpose of providing an indication of the number and scope of applications to be received. A letter of intent is not binding, and it will not enter into the review of any application subsequently submitted, nor is it a necessary requirement for application. This letter should be received no later than February 15, 1983, and sent to:

Dr. Charles L. Turbyfill
National Heart, Lung, and Blood Institute
Westwood Building - Room 553
Betheda, Maryland 20205

B. Format for Applications

Submit applications on form PHS 398, the application form for the traditional research project grant. This form is available in an applicant institution's office of sponsored research or business office or from the Division of Research Grants (DRG). Use the conventional format for research project grant applications and ensure that the points identified in the Section on "Review Procedures and Criteria" are fulfilled.

To identify the application as a response to this RFA, check "yes" on Item 2 of page 1 of the application and enter the title RHEOLOGICAL STUDIES IN SICKLE CELL DISEASE and the RFA number NIH-NHLBI-DBDR-83G-F.

C. Application Procedure

Send or deliver the completed application and six (6) signed, exact photocopies of it to:

Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
Bethesda, Maryland 20205

Send an additional twenty (20) copies of the application to:

Review Branch, DEA
National Heart, Lung, and Blood Institute
National Institutes of Health
Westwood Building - Room 5A15
Bethesda, Maryland 20205

Applications must be received by April 15, 1983. An application not received by this date will be considered ineligible but, after discussion with the applicant, it may be considered as a regular research project grant application.

D. Timetable

Letter of intent	February 15, 1983
Application receipt date	April 15, 1983
Review by the National Heart, Lung, and Blood Advisory Council	September 22-24, 1983
Anticipated award date	September 30, 1983

E. Inquiries

Inquiries regarding this announcement may be directed to the program administrator:

John I. Hercules, Ph.D.
National Institutes of Health
Federal Building - Room 508A
Bethesda, Maryland 20205

Telephone: (301) 496-6931

ANNOUNCEMENT

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

RFA-NIH-NHLBI-DBDR-83G-G

MEGAKARYOCYTOPOIESIS AND THROMBOCYTOPOIESIS

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Application Receipt Date: April 15, 1983

I. PURPOSE

The Division of Blood Diseases and Resources (DBDR)invites grant applications for a single competition for support of research on normal and pathological megakaryocytopoiesis and thrombocytopoiesis. The major purposes of this special grant program are to stimulate the investigation of the differentiation and maturation of the precursor cell to the megakaryocyte and subsequently to the platelet, to determine the characteristics of the regulatory mechanism, and to elucidate the function of the megakaryocyte in various bleeding disorders and in thrombosis. These areas may be approached by studying the differentiation, maturation, morphology, physiology, biochemistry, immunology, and pharmacology of the megakaryocyte.

II. DISCIPLINES AND EXPERTISE

Among the disciplines and expertise that may be appropriate for this research program are biochemistry, immunology, physiology, hematology, and pharmacology.

III. ADMINISTRATIVE BACKGROUND

The Blood Diseases Branch Branch (BDB) of the DBDR supports research on the diagnosis, treatment, and prevention of thrombosis and hemorrhage. One component of the program is platelet disorders, in which the emphasis is on platelet function, metabolism, and development in human and in animal systems. Because there are few projects directed towards studies of megakaryocytopoiesis and thrombocytopoiesis, the Branch is attempting to promote the program and accelerate progress through this RFA.

This program is described in the Catalog of Federal Domestic Assistance No. 13.839, Blood Diseases and Resources. Awards will be made under the authority of the Public Health Service Act, Section 301 (42 USC 241) and administered under PHS grant policies and Federal regulations, most specifically 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

IV. SCIENTIFIC BACKGROUND

The megakaryocyte is a unique cell that occurs only in mammals and that functions primarily to produce platelets. This polyploid cell yields several thousand anucleate platelets through precisely controlled cytoplasmic divisions. The exact mechanism that causes these divisions is not understood. Less is probably known about the megakaryocyte than about any other cell type in the bone marrow, except the stem cell. Among the reasons for this paucity of information is the fact that, over the years, less interest has been shown in megakaryocytes than in the precursors of other blood cells, probably because megakaryocytes constitute less than 0.4 percent of the cellular elements of the bone marrow and because attempts to isolate and concentrate them free of contamination by other cellular elements have only recently been successful.

Recent advances now make it possible to isolate and purify megakaryocytes in large quantities and to study and monitor the megakaryocytes and their precursor cells in culture techniques. Thus, many of the barriers to refined and carefully controlled studies of megakaryocytes have been overcome so that opportunity is available for rapid progress.

V. OBJECTIVES

This special grant program for the support of research in normal and pathological megakaryocytopoiesis and thrombocytopoiesis and the relation between megakaryocytes and thrombotic or hemorrhagic diseases is intended to encourage scientists to investigate the many unanswered questions about megakaryocytes and the production of platelets.

VI. SCOPE

Applications are invited that cover such topics as the morphological, biochemical, and regulatory mechanisms of megakaryocytopoiesis; the cytoplasmic sequestration of megakaryocyte to form platelets; the rate of platelet production; the genesis of platelet organelles; the function of lipid components in controlling the platelet demarcation process and the orientation of new membrane, the function of membrane receptors; and the participation of megakaryocytes in idiopathic thrombocytopenic purpura and other pathological conditions.

VII. MECHANISM OF SUPPORT

The support mechanism for this program will be the traditional, individual research-project grant. Although $500,000 for this program is included in the financial plans for fiscal year 1983, award of grants pursuant to this RFA is contingent upon receipt of funds for this purpose. It is anticipated that four to six grants will be awarded under this program. The specific amount to be funded will, however, depend on the merit and scope of the applications received and the availability of funds.

Upon initiation of the program, the DBDR will sponsor periodic meetings to encourage exchange of information among investigators who participate in this program. In the preparation of the budget for the grant application, applicants should request travel funds for a two-day meeting each year, to be held in Bethesda, Maryland. Applicants should also include a statement in their applications indicating their willingness to participate in such meetings.

The award period for this grant activity must not exceed three years. At the end of the initial award period, renewal applications may be submitted for further competitive review through the regular grant programs of the National Institutes of Health. It is anticipated that support will begin on September 30, 1983.

The current policies and requirements that govern the research grant programs of the National Institutes of Health (NIH) will prevail.

VIII. REVIEW PROCEDURES AND CRITERIA

A. Review Method

All applications responding to this RFA will be reviewed for scientific and technical merit by an initial review group which will be convened by the Division of Extramural Affairs (DEA), National Heart, Lung, and Blood Institute (NHLBI), solely to review these applications. Upon receipt, applications will be reviewed for their responsiveness to the objectives of this RFA. If an application is judged unresponsive, the applicant will be contacted and given an opportunity to withdraw the application or to have it considered for the regular research grant programs of the NIH.

If a proposal submitted in response to this RFA is identical to a research grant application already submitted to the NIH for review, the applicant will be asked to withdraw the pending application before the new one is accepted. Simultaneous submission of identical applications will not be allowed.

B. Review Criteria

The factors to be considered in the evaluation of scientific merit of each application will be similar to those used in the review of traditional research-project grant applications, including the novelty, originality, and feasibility of the approach; the training, experience, and research competence of the investigator; the adequacy of the experimental design; the suitability of the facilities; and the appropriateness of the requested budget to the work proposed. An additional criterion will be the importance of the proposed research to the objectives of this RFA.

IX. METHOD OF APPLYING

A. Letter of Intent

Prospective applicants are encouraged to submit to the Review Branch of the Institute a one-page letter of intent that includes a brief synopsis of the proposed research and identification of any other participating institutions. The Institute requests such letters for the purpose of providing an indication of the number and scope of applications to be received. A letter of intent is not binding, it will not enter into the review of any application subsequently submitted, and it is not a necessary requirement for application.

This letter should be received no later than February 15, 1983, and sent to:

Dr. Charles Turbyfill
National Heart, Lung, and Blood Institute
Westwood Building - Room 553
Bethesda, Maryland 20205

B. Format for Applications

Submit applications on form PHS 398, the application form for the traditional research-project grant. This form is available in an applicant institution's office of sponsored research or business office or from the Division of Research Grants (DRG). Use the conventional format for research-project grant applications and ensure that the points identified in the Section on "Review Procedures and Criteria" are fulfilled.

To identify the application as a response to this RFA, check "yes" on Item 2 of page 1 of the application and enter the title: MEGAKARYOCYTOPOIESIS AND THROMBOCYTOPOIESIS and the RFA number NIH-NHLBI-DBDR-83G-G.

C. Application Procedure

Send or deliver the completed application and six (6) signed, exact photocopies of it to:

Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
Bethesda, Maryland 20205

Send an additional twenty (20) copies of the application to:

Review Branch, DEA
National Heart, Lung, and Blood Institute
National Institutes of Health
Westwood Building - Room 5A15
Bethesda, Maryland 20205

Applications must be received by April 15, 1983. An application not received by this date will be considered ineligible, but, after discussion with the applicant, it may be considered as a regular research-project grant application.

Timetable

Letter of intent	February 15, 1983
Application receite date	April 15, 1983
Review by the National Heart, Lung, and Blood Advisory Council	September 22-24, 1983
Anticipated award date	September 30, 1983

D. Inquiries

Inquiries regarding this announcement may be directed to the program administrator:

Walter R. Miller, M.D.
Blood Diseases Branch
Division of Blood Diseases and Resources
National Heart, Lung, and Blood Institute
National Institutes of Health
Federal Building - Room 5A12
Bethesda, Maryland 20205

Telephone: (301) 496-5911

ANNOUNCEMENT

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

RFA-NIH-NHLBI-DBDR-83G-H

ETIOLOGY, PATHOGENESIS, AND TREATMENT OF APLASTIC ANEMIA

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Application Receipt Date: April 15, 1983

I. PURPOSE

The Division of Blood Diseases and Resources invites grant applications for a single competition for support of research on the etiology, pathogenesis, and treatment of aplastic anemia and related non-neoplastic stem cell disorders.

II. DISCIPLINES AND EXPERTISE

Among the disciplines and expertise that may be appropriate for this research program are epidemiology, cell biology, biochemistry, immunology, toxicology, and clinical medicine.

III. ADMINISTRATIVE BACKGROUND

The Blood Diseases Branch of the Division of Blood Diseases and Resources supports research in red blood cell disorders in order to foster the development of new knowledge for diagnosis, treatment, and prevention. One component of the program is erythropoiesis and stem cell kinetics, in which there is emphasis on aplastic anemia. Because there are few projects directed towards studies of aplastic anemia, the Branch is attempting to promote the program and accelerate progress through this RFA.

IV. SCIENTIFIC BACKGROUND

Non-neoplastic abnormalities in the hematopoietic process may lead to a decrease in the production of one or more of the several cell types produced in the bone marrow. For example, pure red cell aplasia, Diamond-Blackfan anemia, transient erythroblastopenia of childhood, refractory anemia, acquired sideroblastic anemia, and paroxysmal nocturnal hemoglobinuria are diseases associated with suppression of red blood cells. Abnormal erythropoiesis may also result in an overproduction in

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The programs of the National Heart, Lung, and Blood Institute are identified in the Catalog of Federal Domestic Assistance, No. 13.830, Bood Diseases and Resources.Awards will be made under the authority of the Public Health Service Act, Section 301 (42 USC 241) and administered under PHS grant policies and Federal regulations, most specifically 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

the number or function of hematopoietic stem cells, as occurs in polycythemia vera. Neutropenia and thrombocytopenia are deficiences in granulocytes and platelets, respectively. When production of two or more of these cell types is significantly reduced the disease is usually referred to as aplastic anemia. Data suggest an incidence of between 500 and 2,500 cases annually in the United States. It is a serious illness and patients with severe aplasia have a particularly grave prognosis: median survival is less than 6 months and 80 percent of patients die within 1 to 2 years. Survivors rarely improve, and most need continued transfusions of blood products.

Aplastic anemia encompasses a very heterogeneous group of disorders with numerous etiologies and varied natural histories. It can be inherited, but more often it is acquired as a result of reactions to drugs, chemicals, toxins, radiation, or infection. Patients with an inherited predisposition to bone marrow failure are classified as having constitutional aplastic anemia and perhaps the most common disorder in this group is Fanconi's anemia. Patients with Fanconi's anemia are born with one or more of the following characteristic physical abnormalities: hypoplastic thumb or radius, hyperpigmentation, microcephaly, hypoplasia of the kidney and spleen, vision abnormalities, and mental and sexual retardation. Hematologic abnormalities usually develop after the age of five (1).

Unfortunately, the acquired types are frequently idiopathic. The exact mechanisms responsible for bone marrow failure are not yet understood because of the complexity of the hematopoietic system. One can conceive of numerous chances for failure in various stages of hematopoiesis.

While bone marrow transplantation continues to be a rational therapy for some patients with aplastic anemia (2,3), it remains a high-risk procedure, especially for older patients. For most patients with aplastic anemia, bone marrow transplantation is inappropriate. This group includes those who lack histocompatible sibling donors and patients with a moderate form of the disease for whom the risks of transplantation are unwarranted.

Antithymocyte globulin (ATG), a form of therapy directed at the immune system, represents a new and promising clinical treatment for aplastic anemia. This treatment involves injection of ATG or antilyphocyte serum obtained from horses immunized with human thymus lymphocytes. As found in early European trials (4) and in a recent American study (5), therapy with ATG is effective in 30 to 40 percent of patients with severe aplastic anemia.

The mechanism of action of ATG is unknown. Speculation centers on its effect on a pathologic suppressor lymphocyte or killer cell, resulting in suppression of normal hematopoietic development. Alternatively, normal hematopoiesis may require a constant balance between helper and suppressor cell effects, and this balance may be upset in patients with bone marrow failure. The success of ATG therapy and results of numerous recent in vitro studies point to an involvement of the immune system in aplastic anemia. ATG may function by affecting a primary cell-cell interaction or toxic humoral effect or hematologic improvement may be the result of secondary phenomena, such as the ability of serum sickness to stimulate production of hematopoietic factors.

REFERENCES

(1) Schroeder, T.M., Tilgen, D., Kruger, J., Vogel, F.: Formal genetics of Fanconi's anemia. Human Genet 32:257, 1976.

(2) Camitta, B.M., Storb, R., Thomas, E.D.: Aplastic anemia: pathogenesis, diagnosis, treatment, and prognosis. N. Engl. J. Med. 306:645, 712, 1982.

(3) Young, N.: Aplastic anemia: research themes and clinical issues. Progress Hematol 12:227, 1981.

(4) Speck, B., et.al.: Treatment of severe aplastic anemia with anti-lymphocyte globulin or bone marrow transplantation. Brit. Med. J. 282:860, 1981.

(5) Champlin, R., Gale, R.P.: Anti-thymocyte globulin treatment for aplastic anemia: a randomized controlled study. Blood 58:40a, 1981.

V. OBJECTIVES

This special grant program for the support of research on the etiology, pathogenesis, and treatment of aplastic anemia and other non-neoplastic bone marrow abnormalities is intended to encourage scientists to investigate the many unanswered questions about aplastic anemia.

VI. SCOPE

Applications are invited that cover such topics as (but not limited to) the following as they relate to aplastic anemia and other non-neoplastic bone marrow disorders:

- the effects of helper and suppressor T-cells;
- the function of the natural killer cell;
- the involvement of viruses, drugs, chemicals, and toxins;
- the regulation of stem cell differentiation and self-renewal;
- the importance of cell-cell interactions;
- the effect of the bone marrow microenvironment;
- the effects of growth factors and inhibitors;
- the mediation of bone marrow failure by immunological mechanisms;
- the mechanism of action of ATG in treating aplastic anemia; and
- the usefulness of monoclonal antibodies directed against defined T-lymphocyte subsets as a possible alternative to ATG therapy.

VII. MECHANISM OF SUPPORT

The support mechanism for this program will be the traditional, individual research-project grant. Although $500,000 for this program is included in the financial plans for fiscal year 1983, award of grants pursuant to this RFA is contingent upon receipt of funds for this purpose. It is anticipated that four to six grants will be awarded under this program. The specific amount to be funded will, however, depend on the merit and scope of the applications received and the availability of funds.

Upon initiation of the program, the Division of Blood Diseases and Resources will sponsor periodic meetings to encourage exchange of information among investigators who participate in this program. In the preparation of the budget for the grant application, applicants should request travel funds for one two-day meeting each year, to be held in Bethesda, Maryland. Applicants should also include a statement in their applications indicating their willingness to participate in such meetings.

The award period for this grant activity must not exceed three years. At the end of the initial award period, renewal applications may be submitted for further competitive review through the regular grant programs of the National Institutes of Health. It is anticipated that support will begin on September 30, 1983.

The current policies and requirements that govern the research grant programs of the National Institutes of Health will prevail.

VIII. REVIEW PROCEDURES AND CRITERIA

A. Review Method

All applications responding to this RFA will be reviewed for scientific and technical merit by an initial review group which will be convened by the Division of Extramural Affairs (DEA), NHLBI, solely to review these applications. Upon receipt, applications will be reviewed for their responsiveness to the objectives of this RFA. If an application is judged unresponsive, the applicant will be contacted and given an opportunity to withdraw the application or to have it considered for the regular research grant programs of the NIH.

Projects focused on immunologic etiologies or immunologic forms of therapy are of interest to the National Institute of Allergy and Infectious Diseases (NIAID). Applications of this type may be jointly assigned to the NIAID.

Basic research on hematopoiesis which does not emphasize studies on aplastic anemia or other non-neoplastic bone marrow abnormalities may be of interest to the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases (NIADDK) and will be assigned accordingly.

If a proposal submitted in response to this RFA is identical to a research grant application already submitted to the NIH for review, the applicant will be asked to withdraw the pending application before the new one is accepted. Simultaneous submission of identical applications will not be allowed.

B. Review Criteria

The factors to be considered in the evaluation of scientific merit of each application will be similar to those used in the review of traditional research-project grant applications, including the novelty, originality, and feasibility of the approach; the training, experience, and research competence of the investigator; the adequacy of the experimental design; the suitability of the facilities; and the appropriateness of the requested budget to the work proposed. An additional criterion will be the importance of the proposed research to the objectives of this RFA.

IX. METHOD OF APPLYING

A. Letter of Intent

Prospective applicants are encouraged to submit to the Review Branch of the Institute a one-page letter of intent that includes a brief synopsis of the proposed research and identification of any other participating institutions. The Institute requests such letters for the purpose of providing an indication of the number and scope of applications to be received. A letter of intent is not binding, it will not enter into the review of any application subsequently submitted, and it is not a necessary requirement for application.

This letter should be received no later than February 15, 1983, and sent to:

Dr. Charles Turbyfill
National Heart, Lung, and Blood Institute
Westwood Building - Room 553
Bethesda, Maryland 20205

B. Format for Applications

Submit applications on form PHS 398, the application form for the traditional research-project grant. This form is available in an applicant institution's office of sponsored research or business office orfrom the Division of Research Grants (DRG). Use the conventional format for research-project grant applications and ensure that the points identified in the Section on "Review Procedures and Criteria" are fulfilled.

To identify the application as a response to this RFA, check "yes" on Item 2 of page 1 of the application and enter the title: "ETIOLOGY, PATHOGENESIS, AND TREATMENT OF APLASTIC ANEMIA" and the RFA number "NIH-NHLBI-DBDR-83G-H."

C. Application Procedure

Send or deliver the completed application and six (6) signed, exact photocopies of it to:

Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
Bethesda, Maryland 20205

Send an additional twenty (20) copies of the application to:

Review Branch, DEA, NHLBI
National Institutes of Health
Westwood Building - Room 5A15
Bethesda, Maryland 20205

Applications must be received by April 15, 1983. An application not received by this date will be considered ineligible, but, after discussion with the applicant, it may be considered as a regular research-project grant application.

Timetable

Letter of intent	February 15, 1983
Application receipt date	April 15, 1983
Review by the National Heart, Lung, and Blood Advisory Council	September 22-24, 1983
Anticipated award date	September 30, 1983

D. Inquiries

Inquiries regarding this announcement may be directed to the program administrator:

Dr. Alan S. Levine
Red Blood Cell Program Administrator
Blood Diseases Branch
Division of Blood Diseases and Resources
Federal Building - Room 5A12
Bethesda, Maryland 20205

Telephone: (301) 496-5911

ANNOUNCEMENT

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

RFA-NIH-NHLBI-DLD-83G-I

EXTRACELLULAR MATRIX INTERACTIONS IN THE NORMAL AND DISEASED LUNG

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Application Receipt Date: April 15, 1983

I. PURPOSE

The Division of Lung Diseases (DLD), National Heart, Lung, and Blood Institute (NHLBI), invites grant applications for research on the cellular and the biochemical aspects of the extracellular matrix in normal and diseased lung. The objective of this special grant program is to improve our understanding of the role of the interactions of extracellular matrix components in maintaining normal lung functions, changes in the organization and composition of these components in various pulmonary diseases and the subsequent repair processes.

Applications received in response to this request will be reviewed in a single competition.

II. DISCIPLINES AND EXPERTISE

Among the disciplines and expertise that may be appropriate for this research program are cell biology, molecular biology, biochemistry, immunology, cellular physiology, and pulmonary pathology.

III. SCIENTIFIC BACKGROUND

The mammalian lung comprises a number of cell types and subtypes surrounded and supported by extracellular matrices consisting primarily of collagen, elastin, proteoglycans, fibronectin, and other as yet poorly characterized components. These extracellular components are believed to account for many of the mechanical properties of the lung. Recent studies of non-pulmonary systems have clearly demonstrated that the concept of the extracellular matrices as inert supporting materials secreted by cells to serve as mere scaffoldings is no longer valid. They are now perceived as biologically active components of the tissues, in

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This program is described in the Catalog of Federal Domestic Assistance, No. 13.838, Lung Diseases. Awards will be made under the authority of the Public Health Service Act 301 (42 USC 241) and administered under PHS grant policies and Federal regulations, most specifically 42 CFR Part 52 and 45 CFR Part 74. This program i not subject to A-95 Clearinghouse or Health Systems Agency review.

constant communication with cells they surround and capable of influencing metabolism, shape, size and ultimate fate of these cells.

For many types of cells, attachment to collagenous matrix influences growth as well as differentiation. Such interactions of cells with matrix are mediated by glycoproteins which are specific for each cell type and its matrix. For example, attachment of fibroblasts, chondrocytes and epithelial cells is mediated by fibronectin, chondronecin and laminin respectively. These glycoproteins conceivably link specific groups on the matrix molecules with putative receptors on cell surfaces. There is evidence from non-pulmonary systems, that these attachment proteins are more than passive interlocks, and play regulatory roles in cellular functions. Such specific attachment glycoproteins may be similarly associated with lung tissue.

In emphysema, where the pathology is clearly related to the derangement of the pulmonary connective tissue protein elastin, there has been little investigation into the role of matrix interactions in the development of the lesion. Since elastase from the polymorphonuclear leukocytes, which is implicated in the degradation of elastin, also digests other matrix components such as fibronectin, collagens, proteoglycans, etc., these macromolecules may influence elastin degradation.

Examples of specialized extracellular matrices are provided by the basement membranes surrounding epithelial and endothelial cells. Recent studies with glomerular basement membranes suggest that an important function of the alveolar and capillary basement membranes, namely, the regulation of transport of molecules from endothelium to interstitium and from interstitium to alveolus, may be influenced by the interaction among the basement membrane components. Furthermore, alveolar and capillary basement membranes contain anionic components, such as heparan proteoglycans as do glomerular basement membranes and it is possible that "increased permeability" pulmonary edema is analogous to the basement membrane-related permeability changes noted in diseased kidney. The role of pulmonary basement membrane components, individually or in combinations, in the regulation of permeability needs to be better understood.

Extracellular matrix component interactions may also influence the repair processes, by directing the spatial orientation of cells following lung tissue injury. For example, it has long been suspected that the exposed basement membrane, free of attached cells, is somehow responsible for the type II cell proliferation and differentiation associated with lung repair. In experimental emphysema, elastin levels, which decrease following elastase treatment, eventually return to approximately normal levels. However, the new elastin appears to be morphologically abnormal. This could be due to changes either in temporal synthetic sequence of the various matrix components which may prevent development of appropriate interactions or in the controlled degradation of other components.

In recent years considerable information on the biochemistry of individual components of the pulmonary extracellular matrix has become available. However, little is known of their interactions and organization, and neither a plausible structural model of the matrices nor a correlation of biochemical organization with morphology and function have been developed.

IV. OBJECTIVES AND SCOPE

It is the intent of this RFA to encourage study of the roles of the various components of pulmonary extracellular matrix in the maintenance of normal lung function, in the development of physiologic and structural abnormalities in acute and chronic disease states and in induction of subsequent repair processes.

Applications are invited for studies designed to investigate the regulation of biosynthesis and interactions of the pulmonary extracellular matrix components, and their role and fate in disease and repair. Studies may be undertaken in any species but they should have clear relevance to human pulmonary biology and pathology. In all instances, the perceived relationship and importance of the proposed work to the improved understanding of human pulmonary diseases should be made explicit. New approaches and multidisciplinary research efforts are encouraged.

Some unanswered questions relevant to the biology of the pulmonary matrix are listed below in order to provide a perspective of the scope of research that would meet the goals of this program.

A. Matrix Assembly

Even though the synthesis of individual components of extracellular matrices from various organ systems is being elucidated, the total picture of matrix synthesis is far from clear, especially in the lung. To delineate the changes in the amounts and sequential synthesis of the components of the extracellular matrix during disease and repair, a thorough understanding of the factors influencing both the de novo synthesis and turnover of the matrix components is required. Some questions that need to be answered in this regard are: How does the synthesis of matrix by fully differentiated cells differ from that during embryonic development? What are the feedback controls that induce the cells to turn on or off the synthesis of extra cellular matrix components? Is there a temporal sequence for the synthesis of various extracellular matrix components? What is the relationship between molecular and supramolecular structures of extracellular matrix and macroscopic tissue organization and function in normal and diseased lung?

B. Biological Functions

The components of the extracellular matrix are believed to be in constant communication with the cell, influencing the performance and functions of the organ. However, little is known regarding the mechanisms of such communication and function. For example: What are the mechanisms of matrix cell communication in the pulmonary tissue? What is the nature of the receptor(s) on cell surface that react with extracellular matrix components? What is the nature and role of the basement membrane components, alone or in combination, in influencing the alveolar permeability?

C. Disease and Repair

It has been shown that repair processes following tissue injury involve both qualitative and quantitative changes in the extracellular matrix components. A clear understanding of these changes could help development of intervention strategies. The following questions need to be addressed in this regard: What types of perturbations are caused in the interactions of pulmonary matrix components during disease? How do cells respond to such perturbations? What are the roles of the various extracellular matrix components in the repair processes following or during pulmonary disease? What factors prevent normal repair processes or cause misrepair to operate in diseased lung?

It is not required that all of these questions be dealt with in a single proposal. Investigators are encouraged to consider other relevant questions and approaches which would expand our understanding of the role of the pulmonary extracellular matrix in normal and diseased lung.

V. EXCLUSIONS

Studies of nonpulmonary systems, and solely biochemical or morphometric studies of individual components of extracellular matrix exclusive of the nature and effects of their interactions will not be considered responsive to this announcement. Investment of major effort towards isolation of biochemical components or establishment of new cell lines is not encouraged. Studies dealing with lung cancer are also excluded from this program.

VI. MECHANISM OF SUPPORT

The support mechanism for this program will be the traditional, individual, research project grant. Although approximately $800,000 is included for this program in the financial plans for fiscal year 1983, award of grants pursuant to this RFA is contingent upon receipt of funds for this purpose. It is anticipated that six to eight grants will be awarded under this program. The specific amount to be funded will, however, depend on the merit and scope of the applications received and the availability of funds. Since a variety of approaches would represent valid responses to this announcement, it is anticipated that there will be a range of costs among individual grants awarded.

Upon initiation of the program, the DLD will sponsor periodic meetings to encourage exchange of information among investigators who participate in this program. In the preparation of the budget for the grant application, applicants should request travel funds for a one-day meeting each year, most likely to be held in Bethesda, Maryland. Applicants should also include a statement in their applications indicating their willingness to participate.

Applicants should plan and execute their own research programs and are requested to furnish their own estimates of the funds and time required to achieve the objectives of the proposed research project; however, the award period for this activity must not exceed three years. At the end of the initial award period, renewal applications may be submitted for further competitive review through the regular grant period of the NIH. It is anticipated that support will begin on September 30, 1983.

The current policies and requirements that govern the research grant programs of the NIH will prevail, including the requirement for cost sharing.

VII. REVIEW PROCEDURES AND CRITERIA

A. Review Method

All applications submitted in response to this RFA will be reviewed for scientific and technical merit by an initial review group, which will be convened by the Division of Extramural Affairs (DEA), NHLBI, solely to review these applications. Upon receipt, applications will be reviewed for their responsiveness to the objectives of this RFA. If an application is judged unresponsive, the applicant will be contacted and given an opportunity to withdraw the application or permit administrative transfer for consideration in the regular grant program of the NIH.

If a proposal submitted in response to this RFA is identical to a research grant application already submitted to the NIH for review, the applicant will be asked to withdraw the pending application before the new one is accepted. Simultaneous submission of identical applications will not be allowed.

B. Review Criteria

The factors to be considered in the evaluation of scientific merit of each application will be similar to those used in the review of traditional research project grant applications, including the novelty, originality, and feasibility of the approach; the training, experience, and research competence of the investigator(s); the adequacy of the experimental design; the suitability of the facilities; and the appropriateness of the requested budget to the work proposed.

VIII. METHOD OF APPLYING

A. Letter of Intent

Prospective applicants are asked to submit a one-page letter of intent that includes a brief synopsis of the proposed research and identification of any other participating institutions. Such letters are requested for the purpose of obtaining an indication of the number and scope of applications to be received. A letter of intent is not binding, and it will not enter into the review of any application subsequently submitted, nor is it a necessary requirement for application. This letter should be received no later than February 15, 1983, and sent to:

Dr. Charles L. Turbyfill
National Heart, Lung, and Blood Institute
Westwood Building - Room 553
Bethesda, Maryland 20205

B. Format for Applications

Submit applications on form PHS 398, the application form for the traditional research project grant. This form is available in the applicant institution's office of sponsored research or from the Division of

Research Grants (DRG). Use the conventional format for research project grant applications and ensure that the points identified in the section on "Review Procedures and Criteria" are fulfilled.

To identify the application as a response to this RFA, check "yes" on item 2 of page 1 of the application and enter the title "EXTRA MATRIX INTERACTIONS IN THE NORMAL AND DISEASED LUNG" and the RFA number NIH-NHLBI-DLD-83G-I.

C. Application Procedure

Send or deliver the completed application and six (6) signed, exact photocopies of it to:

Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
Bethesda, Maryland 20205

Send an additional twenty (20) copies of the application to:

Review Branch, DEA
National Heart, Lung, and Blood Institute
National Institutes of Health
Westwood Building - Room 5A15
Bethesda, Maryland 20205

Applications must be received by April 15, 1983. An application not received by this date will be considered ineligible.

D. Timetable

Letter of intent	February 15, 1983
Application receipt date	April 15, 1983
Review by National Advisory Council	September 22-24, 1983
Anticipated award date	September 30, 1983

E. Inquiries

Inquiries regarding this announcement may be directed to the program administrator:

Dr. Zakir Bengali
Airways Diseases Branch
Division of Lung Diseases
National Heart, Lung, and Blood Institute
National Institutes of Health
Westwood Building - Room 6A11
Bethesda, Maryland 20205

Telephone: (301) 496-7332

ANNOUNCEMENT

AVAILABILITY OF ANIMALS WITH INHERITED RETINAL DEGENERATIONS

NATIONAL EYE INSTITUTE

The National Eye Institute encourages research directed toward finding the causes of and preventing human heredoretinal degenerations. An NEI contract supports the development of strains of dogs with progressive retinal atrophy and the breeding and distribution of these animals for research purposes. Irish setters exhibiting rod-cone dysplasia and miniature poodles with progressive rod-cone degeneration will continue to be made available to qualified investigators. Investigators interested in obtaining animals are encouraged to contact the NEI. A brief research protocol will be requested and it will be competitively reviewed for scientific merit by a selection committee. There will be no charge for the animals, but shipping and other research related costs will be the responsibility of the individual investigator. For further information please contact:

Jack A. McLaughlin, Ph.D.
Retinal and Choroidal Diseases Branch
National Eye Institute
National Institutes of Health
Building 31 - Room 6A51
Bethesda, Maryland 20205

Telephone: (301) 496-5983

ANNOUNCEMENT

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

RFA-NIH-NHLBI-DHVD-83G-3

SPECIALIZED CENTERS OF RESEARCH IN ISCHEMIC HEART DISEASE (IHD-SCORs)

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

Application Receipt Date: July 18, 1983

I. PURPOSE

The Division of Heart and Vascular Diseases (DHVD) of the National Heart, Lung, and Blood Institute (NHLBI), intends to renew the IHD-SCOR program. These centers include multidisciplinary fundamental and clinical research directed at the reduction of death and disability from ischemic heart disease. The characteristics of Specialized Centers of Research in Ischemic Heart Disease as well as the requirements and format of applications submitted in response to this RFA are covered in subsequent pages. Applications received in response to this request will participate in a single competition. It is open to all interested investigators, those presently involved, and those now interested in participating.

II. DISCIPLINES AND EXPERTISE

This request for grant applications will be of interest to groups engaged in cardiovascular research, particularly those whose investigations include fundamental studies. Investigators in some or all of the following disciplines may wish to participate: biochemistry, biomedical engineering, biophysics, biostatistics, computer sciences, endocrinology, epidemiology, immunology, molecular biology, pathology, pharmacology, and physiology. The request will also be of interest to those involved in clinical investigation of ischemic heart disease, particularly as it relates to the application of basic research findings to the prevention, diagnosis and treatment of myocardial ischemia. Investigators in some or all of the following clinical disciplines may wish to participate: cardiology, radiology, nuclear medicine, and cardiovascular surgery.

This program is described in the Catalog of Federal Domestic Assistance No. 13.837, Heart and Vascular Diseases. Awards will be made under the authority of the Public Health Service Act, Section 301 (42 USC 241) and administered under PHS grant policies and Federal regulations, most specifically 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

III. BACKGROUND

A. The Coronary Heart Disease Program

The Ischemic Heart Disease Specialized Centers of Research (SCORs) are part of the Coronary Heart Disease Program of the DHVD, NHLBI. The Institute and Division have responsibility for the design and administration of research leading to the reduction of death and disability from ischemic heart disease. The Program is intended to foster the development of new knowledge and to support the translation of research results into preventive, diagnostic and therapeutic maneuvers which will have wide clinical application.

The Program supports a wide range of research activities directed towards this goal. These activities cover the research spectrum from fundamental studies to clinical investigations. The mechanisms of support include, in addition to the SCORs, individual research grants, program projects, clinical trials and patient registries.

The SCORs are microcosms of the Program in that they include all aspects of these research activities. SCORs have the advantage that these various activities are coordinated in a single center and across a loose confederation of centers leading to close interaction and rapid dissemination of research findings for the mutual benefit of SCOR investigators, the general cardiovascular community and ultimately the patient with coronary heart disease.

B. History of the SCOR Concept

The IHD-SCORs evolved from the Myocardial Infarction Research Units (MIRU's) which were established in 1967 and expanded in 1968. These units were largely clinical in orientation. Early recognition of the need for balanced fundamental and applied research within centers for the study of ischemic heart disease led to the IHD-SCOR concept. Thus specialized centers were sought in which fundamental and clinical research could be coordinated in a manner that would facilitate the development of new knowledge and its expeditious transfer to prevention and treatment of coronary heart disease.

The first competition for such centers results in the establishment, in 1975, of nine specialized Centers of Research in Ischemic Heart Disease funded for a period of five years. All centers pursued, with varying intensity, both basic and clinical research. A renewal competition in 1979 resulted in the establishment of the curent eight centers; funding for these grants will terminate in 1984.

C. Definition of a SCOR

A Specialized Center of Research (SCOR) is an identifiable unit within a sponsoring institution with a strong commitment to this activity. Each SCOR conducts its own research program based on local interest and talents. Each research program consists of a sustained series of investigations aimed at the reduction of death and disability from ischemic heart disease through better understanding of the etiology and pathogenesis of various ischemic syndromes and ultimately leading to improved prevention, diagnosis and treatment.

A SCOR consists of a cluster of individual, but related, research projects, each with high scientific merit and clear research objectives. A SCOR may address more than one issue; however, a broad range in topics is not a requisite. A SCOR may also include one or more core resources, which perform specialized service activities such as biochemical analysis, pathology, or data management. These activities are shared by several or all investigators. The core investigators, in addition to performing service functions, may also conduct research projects.

Investigators participating in a SCOR must be of recognized ability, capable of conducting independent research, and willing to make long term commitments to the goals of the SCOR. SCOR scientists should have access to facilities where innovative fundamental and clinical investigations can be conducted.

D. SCOR Director

The SCOR Director must provide strong, effective administrative and scientific leadership. The Director is responsible for the organization and operation of the center and for communication with the NHLBI on all scientific and operational matters. The SCOR Director is responsible for maintaining high quality research throughout the five-year funding period. New projects may be incorporated into the program at any time at the discretion of the Director with final review and approval by NHLBI. SCOR grantees are thus encouraged to pursue promising research leads. By the same token, if a Director deems it advisable to discontinue a project, NHLBI staff should be consulted before implementing the decision. Each SCOR Director must encourage and support close collaboration between individual SCOR investigators by means of frequent seminars and scientific meetings.

Each SCOR Director must establish both internal and external advisory committees which will periodically assess the overall program as well as the progress of individual projects. The external advisory committee must consist of expert consultants from outside the grantee institution and must meet annually. The NHLBI program officer may attend their meetings as an observer.

E. Interactions Among SCORS

Active collaboration among the individual SCORs is a most important aspect of the SCOR program. SCOR Directors meet at least once each year to review progress, discuss common problems, and plan collaborative efforts. An annual meeting of SCOR investigators is coordinated by NHLBI and the SCOR Directors. The purpose of the meeting is to encourage exchange of information among SCOR investigators, and to help plan future directions. Topics for formal presentation by SCOR investigators are chosen by the Directors and NHLBI staff.

F. Relation to the NHLBI

A SCOR is a grant-in-aid which differs from other research grants in its goal orientation. The award of a SCOR grant will establish a special relation between the NHLBI and the grantee institution. The NHLBI will designate a scientific program officer who will monitor the program and when necessary provide advice to the Director and staff of each SCOR.

Scientific progress will be evaluated annually by the Institute by review of progress reports included in noncompeting renewal applications. Interim evaluations will also be conducted by the DHVD.

IV. OBJECTIVES AND SCOPE

This solicitation for applications for SCORs on ischemic heart disease emphasizes a continuing trend in the SCOR program toward the inclusion of more research that is directed toward the elucidation of fundamental mechanisms involved in the manifestations and sequelae of myocardial ischemia. Therefore, the proposed program should include fundamental as well as clinically oriented research and should provide for a mutually supportive interaction between the basic scientists and clinical investigators. The individual projects should be correlative or complementary in terms of the topic or topics chosen within the general area of ischemic heart disease. It is hoped that new applicants will participate in the competition and that it will be possible to fund some smaller centers. It is unlikely, however, that an application with less than three projects would be responsive. Emphasis in proposed projects should be on the development of innovative approaches, the elaboration of new and significant hypotheses, and the generation of novel strategies to resolve current issues.

The unsolved problems in research related to ischemic heart disease are many. A catalog of these prolems would be lengthy and probably not useful in this document. The following brief discussion of research topics is intended to offer a few examples of the kinds of research sought and to emphasize the importance of fundamental, new, and innovative research in this second renewal of the IHD-SCOR program.

Many basic structural and functional charcteristics of the coronary circulation, both large and small vessels, under normal and hypoxic conditions are poorly understood. The pathophysiology of ischemic injury, the time course, and means to modify and prevent severe ischemic injury and necrosis in the coronary circulation itself are important research topics. The roles of coronary endothelial injury, spasm and thrombosis in the genesis of acute ischemic events are poorly understood. The therapeutic control of inadequate coronary flow during acture ischemia might be a clinically oriented project of importance to pursue in parallel with basic studies.

Topics of substantial importance are the mechanisms involved in triggering acute ischemic events such as sudden cardiac death and acute infarction with or without associated coronary occlusion. The local and systemic factors leading to acute thrombosis and spasm in epicardial coronary arteries are only dimly perceived. Refinement of diagnostic technique to predict the likelihood of acute events and to promote understanding of the etiology and pathophysiology of such events would be of value in the design of new preventive and therapeutic maneuvers. Both fundamental and applied studies are needed in this area.

The development of collateral vessels in response to chronic ischemia, and following an acute event is of interest, particularly with regard to the mechanisms which initiate the process. The factors which lead to exuberant collateral development in some individuals and the paucity of such vessels in others are unknown and involve fundamental biologic processes such as growth and differentiation. Elucidation of control mechanisms might ultimately permit endogenous bypass of epicardial coronary lesions.

While the study of heart function has produced much new knowledge in recent years, these advances have uncovered many areas that demand further study, particularly at the cellular level. The sequence of events leading from reversible to irreversible damage of the heart muscle cell in ischemia needs further elucidation in order to design more effective pharmacologic modalities for interruption of this process. For example, further studies are needed of ischemic metabolic changes and the manner in which ischemic conditions modify the contractile and electrophysiologic properties of cardiac tissue. Another example concerns the role of various subcellular organelles in maintaining these properties and the role which impaired function of these organelles plays in the development of irreversible damage to heart muscle cells. Therapy designed to protect the integrity of cellular organelles might be pursued both in the laboratory and the clinic.

Disturbances in protein synthesis and degradation in heart muscle as a result of acute or chronic oxygen or substrate deprivation may play a role in the loss of contractile function. Little attention has been paid to the factors in ischemia which might disturb the balance of protein turnover. Moreover little attention has been paid to cardiac hypertrophy which results from chronic myocardial ischemia. Hypertrophy is a fundamental biologic process which is poorly understood.

The relationship of the nervous system to cardiac function under normal and ischemic conditions is an important topic for further fundamental research. Central nervous system effects upon the coronary circulation and heart function are not well understood. Furthermore, information on the effect of central nervous system stimulation of the ischemic heart and whether this is a significant factor leading to arrhythmias and sudden death is of paramount importance in view of the continued prevalance of instantaneous sudden cardiac death and the fact that under the best of circumstances only 20-40 percent survive this catastrophic event. The importance of fundamental understanding of these processes is crucial to effective preventive efforts.

Much remains unknown concerning the complex mechanisms which mediate control of the heart by both the sympathetic and parasympathetic limbs of the autonomic nervous system. The manner in which this control may be exerted by various biochemical entities at the cellular and molecular level to affect contractile and electrophysiological properties requires further clarification. This is of particular importance given the recent clear demonstration that beta-blockade reduces mortality in survivors of myocardial infarction.

The clinicopathologic features of various ischemic heart disease syndromes need to be further clarified in order to define risk groups, to develop prognostic criteria and ultimately to design and evaluate pharmacologic interventions. Topics of current interest include continuing efforts to reduce oxygen demand by the heart while maintaining function, the maintenance of an adequate energy supply in the face of hypoxia and the control of cellular injury and the inflammatory process. These are examples of areas where the results of basic findings are close to providing new leads for the treatment of patients.

V. EXCLUSIONS

No support will be provided for large clinical trials or for programs containing exclusively clinical studies or fundamental studies without at least one clinically oriented project. While the development of new instrumentation may be a part of the SCOR, support for development alone, will not be funded. Similarly, funds will not be provided for the purchase and installation of very expensive, new equipment. Institute staff should be consulted if an applicant has questions regarding this limitation.

VI. MECHANISM OF SUPPORT

The support mechanism will be the research grant-in-aid for a period of five years commencing January 1, 1985. However, it will differ from other research grants in the expected communication between centers and periodic structured review of progress by the NHLBI.

Applicants are expected to furnish their own estimates of the time required to achieve specific objectives of the proposed work, a schedule for completion of the work, and an outline of the phases or segments into which the proposed program can be logically divided. The IHD-SCOR will plan, direct and execute its own research program, but any substantial modifications in it must be mutually agreed upon by the IHD-SCOR institution and the NHLBI.

Additionally, a yearly two-day meeting of SCOR investigators will be held, most likely in Bethesda, Maryland, and applicants should include a request for travel funds for this meeting in each year of the budget. Applicants should also include a statement in the application indicating willingness to participate in such meetings.

Although this solicitation is included in the plans for Fiscal Year 1985, support of grants pursuant to this request for applications is contingent upon ultimate receipt of appropriate funds for this purpose. The current program includes eight grants which have a total annual funding base of approximately $13 million (including indirect costs). At this time, it is not possible to predict whether future funding will be at the current level or at a lower level. This will be influenced by the amount of funds available to the Division, by the overall merit of proposals, and by their relevance to the program objectives. It is the intent of this solicitation to include some smaller centers and to emphasize fundamental, new, innovative research. A variety of approaches would be responsive to this solicitation; accordingly, it is anticipated that there will be a range of costs among individual grants awarded.

VII. REVIEW PROCEDURES AND CRITERIA

The applications will be evaluated in national competition with each other. Primary review will be conducted by a review group of predominantly non-federal consultants with selected scientific expertise and may involve a site visit. Secondary review will be by the National Heart, Lung, and Blood Advisory Council

Applications considered non-responsive will be returned to the investigator. Major factors to be considered in the evaluation of responsive applications will include:

1. The scientific merit of each proposed project, including the novelty, originality and feasibility of the approach and the adequacy of the experimental design;
2. The technical merit and justification of each core unit;
3. The competence of the investigators to accomplish the proposed research goals, their commitment, and the time they will devote to the program;
4. The adequacy of facilities to perform the proposed research including the laboratory and clinical facilities and the proposed instrumentation and data management systems, when needed;
5. The integration of the various projects and core units into an effective center, and the adequacy of plans for interaction and dissemination of information among investigators;
6. The qualifications, experience and commitment of the SCOR Director and the ability to devote adequate time and effort to provide effective leadership to the center;
7. The scientific and administrative structure of the program, including adequate internal and external procedures for monitoring the proposed research and for providing ongoing quality control and scientific review;
8. The institutional commitment to the program, and the appropriateness of its resources and policies for the administration of a research program of the type proposed;
9. The willingness to work cooperatively with other Specialized Centers of Research in Ischemic Heart Disease and with the NHLBI; and
10. The appropriateness of the budget for the proposed program.

VIII. METHOD OF APPLICATION

A. Letter of Intent

Prospective applicants are encouraged to submit a one-page letter of intent which includes a synopsis of proposed areas of research and identification of any other participating institutions. This letter should be received no later than April 4, 1983, and should be addressed to:

Dr. Charles L. Turbyfill
Division of Extramural Affairs
National Heart, Lung, and Blood Institute
National Institutes of Health
Westwood Building - Room 553
5333 Westbard Avenue
Bethesda, Maryland 20205

The Institute requests such letters only to provide an indication of the number and scope of applications to be received. A letter of intent is not binding, and it will not enter into the review of any proposal subsequently submitted, nor is it a necessary requirement for application.

B. Application Procedure

In addition to the signed original and six copies to be mailed to the Division of Research Grants (DRG) (see PHS 398 instructions p. 8), three copies should be sent or delivered to:

Review Processing Section
Division of Extramural Affairs
National Heart, Lung, and Blood Institute
National Institutes of Health
Westwood Building - Room 5A15
5333 Westbard Avenue
Bethesda, Maryland 20205

To ensure their review, applications must be received by July 18, 1983

C. Format for Applications

Form PHS 398 (Revised May 1982) should be used, but since this form is used primarily for the traditional project-grant application, several sections have to be modified and expanded so that this form can be used to provide the additional information needed for the Ischemic Heart Disease Specialized Centers of Research Application.

A SPECIAL SUPPLEMENT IS AVAILABLE CONTAINING SPECIFIC GUIDELINES FOR THE PREPARATION OF AN IHD-SCOR APPLICATION. PROSPECTIVE APPLICANTS SHOULD SUBMIT A WRITTEN REQUEST FOR THESE GUIDELINES TO THE PROGRAM OFFICIAL LISTED BELOW.

D. Timetable

Letter of intent	April 4, 1983
Application receipt date	July 18, 1983
Review by the National, Heart, Lung, and Blood Advisory Council	May 17-19, 1984
Notification of applicants	May 25, 1984
Anticipated award date	January 1, 1985

IX. INQUIRIES

Inquiries about the Ischemic Heart Disease SCOR program should be addressed to:

Eugene R. Passamani, M.D.
Associate Director for Cardiology, DHVD
National Heart, Lung, and Blood Institute
National Institutes of Health
Federal Building - Room 3C12
Bethesda, Maryland 20205

Telephone: (301) 496-1081

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